CENTRAL LIBRARY
Birla Institute of Technology & Science
PILANI (Rajasthan)

Call No. 543.8
S458T
V.2
Accession No. 33694

Acc. NO...............

ISSUE LABEL

Not later than the latest date stamped below.

THE TERPENES

VOLUME II

THE TERPENES

VOLUME II

The Dicyclic Terpenes and their Derivatives

BY

J. L. SIMONSEN

SECOND EDITION REVISED

BY

SIR JOHN SIMONSEN, D.SC. (MANC.), F.R.I.C., F.R.S.
Director of Research, Colonial Products Research Council
Formerly Professor of Chemistry, University College of
North Wales, Bangor

AND

L. N. OWEN, B.SC., PH.D. (BIRM.), F.R.I.C.
Lecturer in Organic Chemistry, Imperial College of
Science and Technology, South Kensington

CAMBRIDGE
AT THE UNIVERSITY PRESS
1949

PUBLISHED BY
THE SYNDICS OF THE CAMBRIDGE UNIVERSITY PRESS
London Office: Bentley House, N.W. 1
American Branch: New York
Agents for Canada, India, and Pakistan: Macmillan

First Edition 1931
Second Edition 1949

Printed in Great Britain at the University Press, Cambridge
(Brooke Crutchley, University Printer)

PREFACE

In the first section of this volume the chemistry of the dicyclic terpenes and their derivatives are surveyed. Few, if any, natural products have formed the subject of such intensive study as the pinenes and camphor. It is obviously impossible within the limits of a monograph to refer to every memoir, but it is hoped that no investigations of importance have been omitted. It has been considered desirable to include a brief account of Robinson's interpretation of the mechanism of the Wagner rearrangement, since this explains in a simple and satisfactory manner many of the most puzzling problems in the chemistry of camphor.

Owing to their close relationship to many substances of outstanding biochemical interest, special importance attaches to the sesquiterpenes, which are discussed in Section II. Within the last decade, thanks to the brilliant investigations of Ruzicka and his collaborators, their chemistry has been gradually elucidated, but much remains to be accomplished. No attempt has been made to refer to all the sesquiterpenes, which have been described in the literature, and only those which appear to be definitely homogeneous have been discussed.

The writer is indebted to Professor R. Robinson, F.R.S., for revising the text dealing with the Wagner rearrangement, and his especial thanks are due to Professor C. S. Gibson, O.B.E., F.R.S. and Dr R. S. Cahn, who have once again undertaken the labour of reading the proofs.

J. L. S.

BANGOR
March 1932

PREFACE TO THE SECOND EDITION

During the eighteen years which have elapsed since the publication of the first edition, our knowledge of the chemistry of the dicyclic terpenes and the sesquiterpenes has greatly increased. It has been found desirable, therefore, to devote this volume to the chemistry of the dicyclic terpenes, and to include in a third volume the sesquiterpenes and diterpenes.

Literature has been consulted up to the close of 1947 and it has been found possible to include also some references to work published in 1948.

We are once more indebted to Lt.-Col. H. J. Holman, B.Sc., A.R.C.S., for undertaking the laborious task of checking all the literature references.

J. L. S.
L. N. O.

LONDON, 1948

CONTENTS

THE DICYCLIC TERPENES AND THEIR DERIVATIVES

Introduction . . . . . . page 1

CHAPTER I. THUJANE AND ITS DERIVATIVES

A. Hydrocarbons:

Thujane 5
α-Thujene 10
β-Thujene 14
Sabinene 16

B. Alcohols:

Thujyl Alcohol 23
Sabinol 28

C. Ketones:

Thujone 32
Umbellulone 52

CHAPTER II. CARANE AND ITS DERIVATIVES

A. Hydrocarbons:

✓Carane 61
Δ^3-Carene 64
Δ^4-Carene 73

B. Ketones:

Carone 77
Eucarvone 85

C. Oxide:

Δ^3-Carene-5:6-epoxide 95

CHAPTER III. PINANE AND ITS DERIVATIVES

A. Hydrocarbons:

Pinane . . . . . *page* 100
α-Pinene 105
Oxidation of α-Pinene . . . 136
Molecular Rearrangements of α-Pinene and Related Compounds . . . 156
General Reactions of α-Pinene . . 165
β-Pinene (Nopinene) 191

B. Alcohols:

Pinocampheol 205
Myrtenol 210
Verbenol 214
Pinocarveol 220

C. Aldehyde:

Myrtenal 223

D. Ketones:

Pinocamphone 226
Verbenone 232
Pinocarvone 240

CHAPTER IV. SANTENE AND ITS DERIVATIVES

A. Hydrocarbon:

Santene 243

B. Alcohols:

The Santenols 251
Santene Hydrate 256

C. Ketone:

Santenone (π-Norcamphor) . . . 257

D. Related Tricyclic Compounds:

Teresantalol and Teresantalic Acid . . 264

CHAPTER V. CAMPHANE, *ISO*CAMPHANE AND THEIR DERIVATIVES

A. Hydrocarbons:

Camphane . . . . *page* 272
*iso*Camphane (Dihydrocamphene) . . 275
Camphenilane 278
Camphene 280
Bornylene 322
Apobornylene 331
Tricyclene (Cyclene) 333
Bornyl and *iso*Bornyl Chlorides . . . 340

B. Alcohols:

Borneol 349
*iso*Borneol 365

C. Ketones:

Camphenilone 367
Camphor 373
  The Halogen Derivatives of Camphor . 395
  Nitrocamphor and its Derivatives . . 410
  The Camphor-Sulphonic Acids . . 419
  The Hydroxycamphors . . . 427
  Some Reactions of Camphor Involving the Carbonyl Group 433
  Some Reactions of Camphor Involving the α-Carbon Atom 447
  Camphorquinone 466
  Camphoric Acid 478
    Some Degradation Products of Camphoric Acid 502
Epicamphor (β-Camphor) . . . 512
Interconversion of Enantiomorphs in the Camphor Series 522

CHAPTER VI. FENCHANE, *ISO*BORNYLANE AND THEIR DERIVATIVES

A. Hydrocarbons:

Fenchane . . . . *page* 526
*iso*Bornylane 528
The Fenchenes 531
α-Fenchene 538
β-Fenchene 543
γ-Fenchene 547
δ-Fenchene 548
ζ-Fenchene 549
*cyclo*Fenchene 550

B. Alcohols:

Fenchyl Alcohol 552
*iso*Fenchyl Alcohol 557

C. Ketones:

Fenchone 560
*iso*Fenchone 580

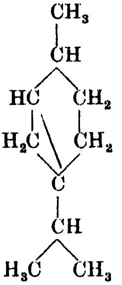
INDEX OF AUTHORS 589

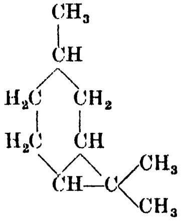
INDEX OF SUBJECTS 600

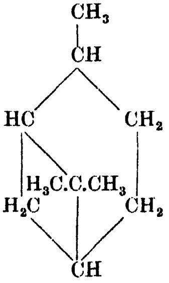
THE DICYCLIC TERPENES AND THEIR DERIVATIVES

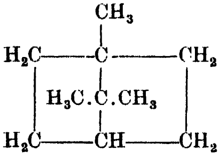
INTRODUCTION

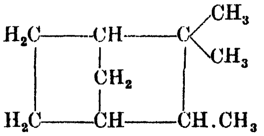
The dicyclic terpenes, containing ten carbon atoms, are derivatives of the saturated hydrocarbons thujane (I), carane (II), pinane (III), camphane (IV), *iso*camphane (V), fenchane (VI) and *iso*bornylane (VII).

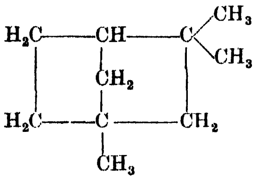

(I)

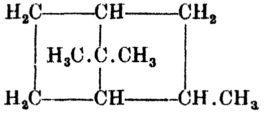

(II)


(III)

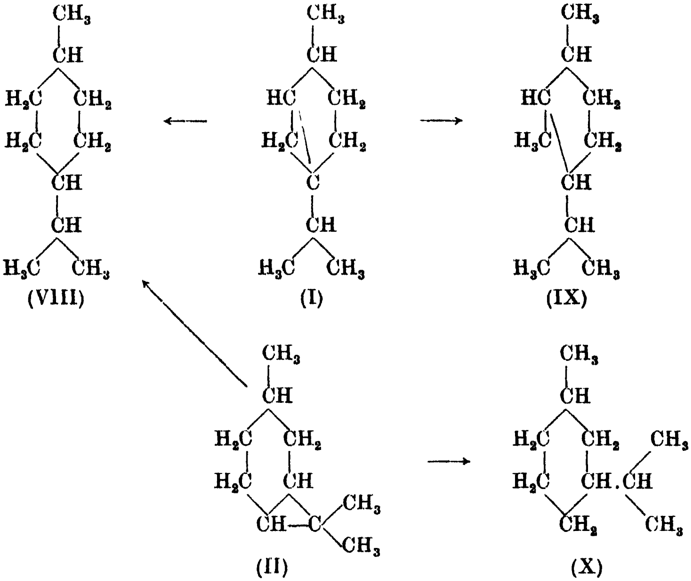

(IV)


(V)


(VI)


(VII)

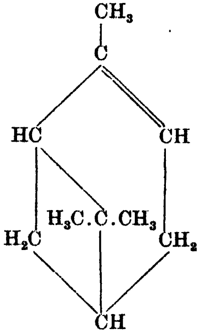
The determination of the constitution of the terpenes derived from thujane and carane has afforded comparatively little difficulty, since they show little tendency to react abnormally. The dicyclic ring structures can in each case undergo fission in two directions; thus thujane can give rise to derivatives of either *p*-menthane (VIII) or "Isothujan" (IX) (compare footnote ‡, p. 39) and carane to those of *p*-menthane (VIII) and *m*-menthane (X). As will be seen, fission in both directions does actually occur.



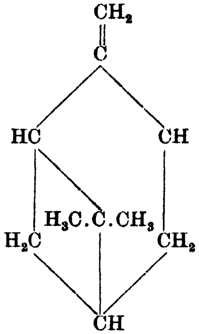
α-Pinene (XI) and β-pinene (XII) may be regarded as the parent hydrocarbons of all the terpenes, since they can pass by ring fission into dipentene (XIII) and other monocyclic terpenes, and by molecular rearrangement into borneol (XIV) and other substances containing the camphane nucleus. Since borneol yields camphene (XV) on dehydration, the very close relationship of the dicyclic structures represented by (III), (IV), and (V) is obvious.

This tendency for molecular rearrangements to occur, involving a complete change in ring structure, has added greatly to the difficulties encountered in the study of the chemistry of these substances. The mechanism involved in these changes, for which Robinson has provided a theoretical explanation, is discussed later.

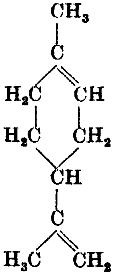
Difficulties of the same kind have been met with in the chemistry of the derivatives of fenchane and *iso*bornylane, both of these dicyclic rings showing a marked tendency to undergo the Wagner rearrangement.



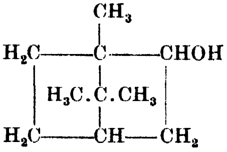
(XI)



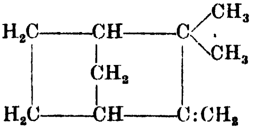
(XII)



(XIII)



(XIV)

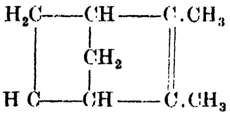


(XV)

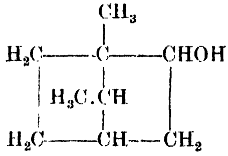
One dicyclic hydrocarbon, santene (XVI), containing nine carbon atoms, has been found in nature, and its occurrence has been used* as an argument, in the writers' opinion erroneously, against the isoprene theory of the structure of the terpenes. It would appear to be improbable that santene is a primary plant product, and it seems not unlikely that it is formed from santenol (or the related ketone, santenone) (XVII) by a Wagner rearrangement. The alcohol itself can result from the decarboxylation and hydration of teresantalic acid (XVIII). These changes have been realised experimentally, and it is not without significance

* Mitter, *J. Ind. C.S.* 1930, **7**, 39. Mitter's statement, that sylvestrene is a natural product, is unsupported by any fresh experimental evidence, and his final argument, that santonin is not an isoprene derivative, has been shown to be incorrect by the synthetical investigations of Clemo, Haworth and Walton (*J.C.S.* 1929, p. 2368.

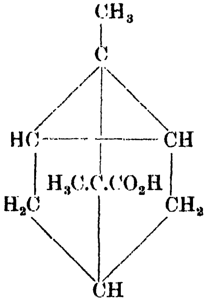
that teresantalic acid, santenol and santene all occur in East Indian sandalwood oil.



(XVI)



(XVII)



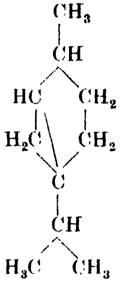
(XVIII)

CHAPTER I

THUJANE AND ITS DERIVATIVES

A. HYDROCARBONS

THUJANE



The dicyclic hydrocarbon *d*-thujane[*] (tanacetane or dihydrosabinene), $C_{10}H_{18}$ (IV), was first described by Tschugaev and Fomin,[†] who prepared it by the catalytic hydrogenation of l-*α-thujene* (I), d-*β-thujene* (II) and d-*sabinene* (III) in the presence of platinum black, using a pressure of 25 atmospheres. At the same time Kishner[‡] obtained *d*-thujane by the distillation of d-iso*thujonehydrazone* (V) with potassium hydroxide, whilst some years later Semmler and Feldstein[§] prepared it from this derivative by the action of sodium ethoxide at 145°. According to Henderson and Robertson[‖] it is also formed in small amount when sabinol is hydrogenated in the presence of platinum black.

Kishner also claimed to have prepared thujane by the oxidation with potassium ferricyanide of *thujylhydrazine* (VI) which can be obtained by the reduction of the hydrazone with sodium and alcohol, but it is probable that the hydrocarbon produced in this reaction is 1:2-dimethyl-3-*iso*propyl*cyclo*pentane (see p. 13).

---

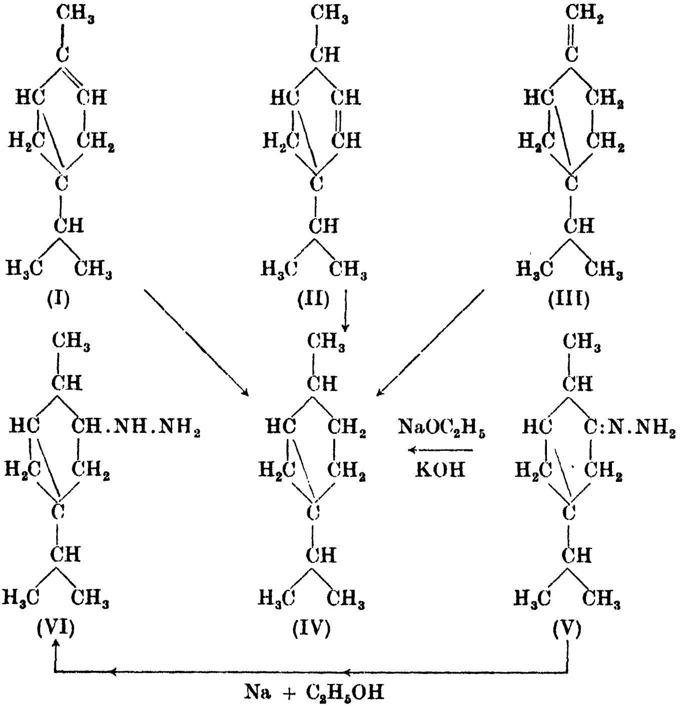
[*] Seyler (*Ber.* 1902, **35**, 550) separated from oil of sage a hydrocarbon, salvene, b.p. 142–145°, which he considered to have the formula now known to be that of thujane. The actual constitution of this hydrocarbon is not known.

[†] *Compt. rend.* 1910, **151**, 1058; compare Richter, Wolff and Presting, *Ber.* 1931, **64**, 876.

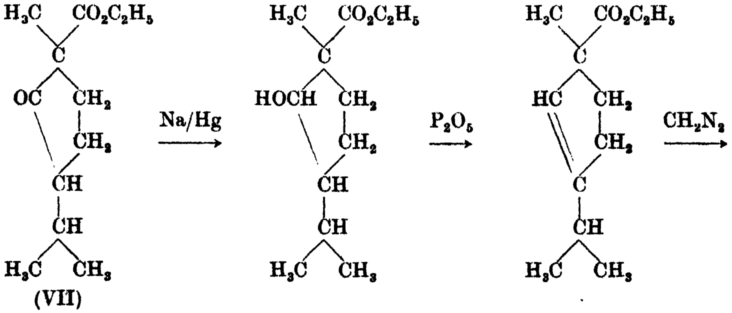
[‡] *J. Russ. Phys. Chem. Soc.* 1910, **42**, 1198.

[§] *Ber.* 1914, **47**, 387.

[‖] *J.C.S.* 1923, **123**, 1713; compare Birch, *ibid.* 1945, p. 811.

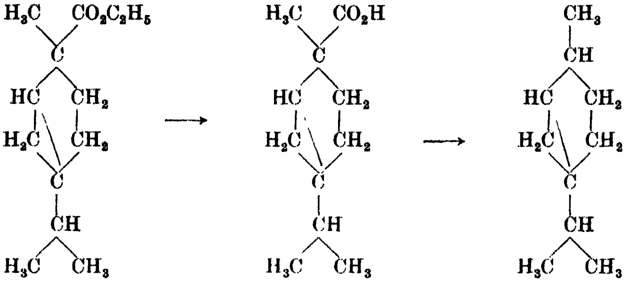


dl-Thujane has been synthesised by Guha and Krishnamurthy * from ethyl 1-methyl-3-*iso*propyl*cyclo*pentan-2-one-1-carboxylate (VII) by the following route:



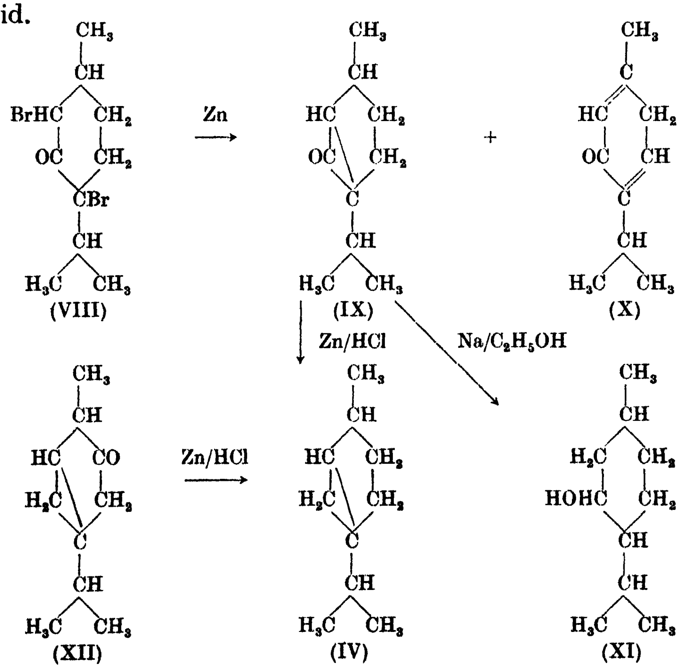
---

* *Ber.* 1937, **70**, 2112.



(IV)

Another synthesis* is based on 2:4-dibromomenthone (VIII) which on treatment with zinc dust in alcohol gives a mixture of the *ketothujane* (IX) and 1-methyl-4-*iso*propyl*cyclo*hexadien-3-one (X). The ketothujane, which is isomeric with thujone, has b.p. 110–112°/14 mm., $d_{4^\circ}^{23^\circ}$ 0·9010, n_D 1·4505, $[\alpha]_D^{27^\circ} + 25^\circ$, and gives two *semicarbazones*, (i) m.p. 175–176° and (ii) m.p. 150–151°, both of which show the same specific rotation $[\alpha]_D^{26^\circ} - 53^\circ$ in acetic acid.



(VIII) (IX) (X) (XII) (IV) (XI)

---

* Guha and Nath, *Ber.* 1937, **70**, 931.

Reduction of the ketone with sodium and alcohol takes place with ring scission to give menthol (XI), but by the Clemmensen method it gives thujane (IV), b.p. 156–157°, $d_{4°}^{22°}$ 0·8140, $n_D^{20°}$ 1·4410, $[\alpha]_D^{20°} + 8·5°$. Apart from the low specific rotation, these physical constants are in good agreement with those observed for a specimen of the hydrocarbon, b.p. 155–156°, $d^{20°}$ 0·8120, $n_D^{20°}$ 1·4435, $[\alpha]_D^{20°}$ +49·4°, prepared by Clemmensen's reduction of *d-iso*thujone (XII). For the hydrocarbon prepared from *l*-α-thujene Tschugaev and Fomin quoted the constants b.p. 157°/758 mm., $d_{4°}^{20°}$ 0·8139, $n_D^{20°}$ 1·4375, $[\alpha]_D$ +62·03°. The calorific value, determined by Roth and Ostling* is 1508·6 kg.-cals.

Thujane, a colourless mobile oil, with a faint odour, gives no characteristic crystalline derivatives suitable for its identification. According to Zelinski and Kasansky its solution in acetic anhydride gives a bright red colour with concentrated sulphuric acid, a reaction also shown by α-thujene.

When distilled over palladinised charcoal at 160–162° in a current of hydrogen, *d*-thujane gives 1:2-*dimethyl*-3-iso*propyl*-cyclo*pentane* (XIII),† b.p. 159·5–160·5°/771 mm., $d_{4°}^{17°}$ 0·7910, $n_D^{17°}$ 1·4344, a hydrocarbon which had been prepared previously by Kishner (see below). Zelinski and Lewina‡ have shown that *d*-thujane is isomerised when distilled in a current of carbon dioxide over platinised charcoal at 300°. The hydrocarbon, $C_{10}H_{18}$, b.p. 163·5–164·5°, n_D 1·4452, is considered to have one of the formulae (XIV), (XV), or (XVI), but no direct proof of its constitution has been obtained.

Thujane reacts very slowly with potassium permanganate in the cold but, on warming, oxidation occurs to give *α-methyl-α'*-iso*propyladipic acid* (XVII).§

The tendency for thujane to yield *cyclo*pentane derivatives exemplified above is also shown in its reaction with bromine and hydrogen bromide. According to Kishner‖ it reacts readily with bromine to give an unstable *dibromide*, $C_{10}H_{18}Br_2$, the addition of bromine being evidently accompanied by ring fission. The constitution of this substance, together with that of the hydrocarbon $C_{10}H_{18}$, obtained from it by the action of alkali, has not been determined.

---

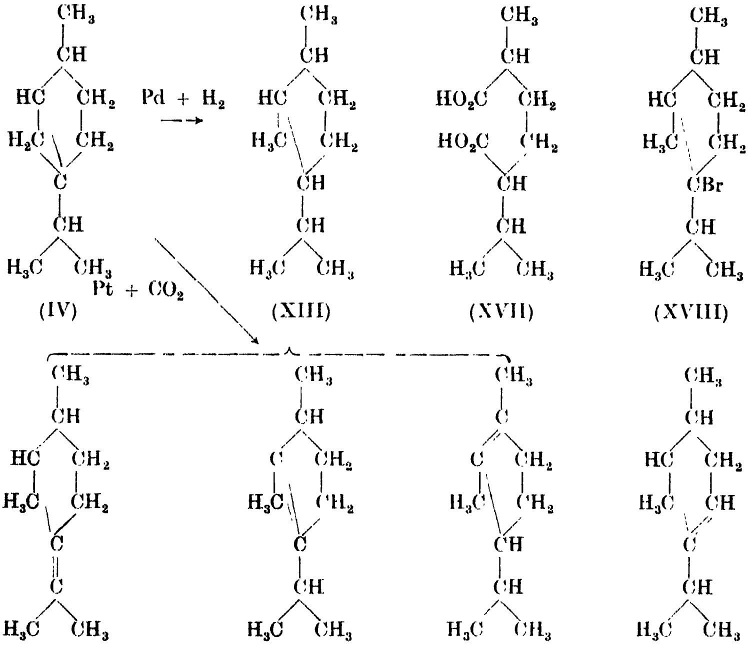
* *Ber.* 1913, **46**, 323.

† Zelinski and Kasansky, *Ber.* 1927, **60**, 1098.

‡ *Annalen*, 1929, **476**, 65.

§ Guha and Krishnamurthy, *loc. cit.*

‖ *J. Russ. Phys. Chem. Soc.* 1910, **42**, 1198; 1911, **43**, 1157.



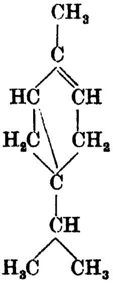
(IV) (XIII) (XVII) (XVIII)

(XIV) (XV) (XVI) (XIX)

With hydrogen bromide in acetic acid solution the nature of the product depends upon the time allowed for the reaction to proceed. After two days an unstable *hydrobromide*, $C_{10}H_{19}Br$, is obtained, whilst after two months a stable hydrobromide of the same composition can be separated. Kishner considers that these two bromides are probably *cis-trans*-isomerides, having the structure represented by (XVIII). The stable bromide does not react with alkali, but when digested with quinoline it gives an unsaturated *hydrocarbon*, $C_{10}H_{18}$, b.p. 162–164°/755 mm. A hydrocarbon having very similar constants, b.p. 163–164°, $d_{5^\circ}^{18^\circ}$ 0·8131, n_D 1·4540, $[\alpha]_D$ +2·88°, can be prepared by the action of alkali on the unstable bromide, whilst by the interaction of thujane with hydrogen iodide followed by treatment of the hydriodide with alkali, a third hydrocarbon, b.p. 162–163°/742 mm., $d_{0°}^{20°}$ 0·8105, n_D 1·4527, $[\alpha]_D$ +0·22°, is obtained. There can be little doubt that these three hydrocarbons are identical and, assuming them to be homogeneous, they must be represented by one of the formulae (XIV), (XV), or (XIX). On hydrogenation by the Sabatier-Senderens process[*] they yield 1:2-*dimethyl*-3-iso*propyl*cyclo*pentane* (XIII), the constitution of which has been established by Kasansky.[†]

Thujane may be heated with sulphuric acid (1:6) at 140° without undergoing any change (Kishner), but it is resinified by the concentrated acid and reacts with violence with nitric–sulphuric acid mixture (Zelinski and Kasansky).

α-*THUJENE*



Although *l*-α-thujene was prepared by Tschugaev[‡] in 1900 by methods to be described, the occurrence of *d*-α-thujene in nature was first observed in 1923, when Simonsen[§] showed it to be the chief constituent present in the terpene fraction of the oil derived from the gum-oleo-resin of *Boswellia serrata* Roxb. It is only recently, however, that Birch and Earl[||] have shown that the hydrocarbon "*origanene*" is a mixture of *d*- and *dl*-α-thujene. Origanene was first isolated in 1908 by Pickles[¶] from Cyprus origanum oil, who gave the physical constants b.p. 160–164°, $d^{16°}$ 0·847, n_D 1·480, and described a *nitrosochloride* decomposing at 91–94°, d-*nitrolpiperidide*, m.p. 198°, and a *nitrolbenzylamine*, m.p. 104–105°. Birch[*] isolated the same hydrocarbon from *Eucalyptus dives*, and it was from a further examination of this material that its identity was eventually established.

---

[*] Kishner, *J. Russ. Phys. Chem. Soc.* 1912, **44**, 1759.

[†] *Ber.* 1929, **62**, 2205.

[‡] *Ibid.* 1900, **33**, 3120; 1901, **34**, 2276.

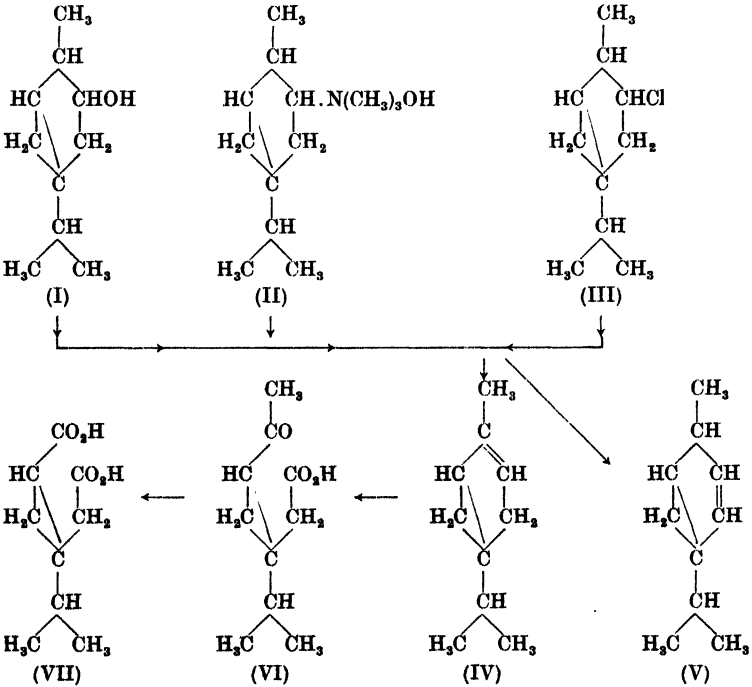
[§] *Ind. For. Rec.* 1923, **9**, 289.

[||] *J. Proc. Roy. Soc. New South Wales*, 1939, **72**, 55.

[¶] *J.C.S.* 1908, **93**, 862; compare Henry and Paget, *J.C.S.* 1931, p. 25.

It was found by Tschugaev that when the *methylxanthate* of *thujyl alcohol* (I) or *thujyltrimethylammonium hydroxide* (II) was distilled, a mixture of hydrocarbons was obtained which could be separated into two main fractions, (i) b.p. 147·5–149·5° and (ii) b.p. 152–152·5°. The latter, which was formed in larger quantity, was designated *α-thujene* and the former *β-thujene*. Contemporaneously, Kondakov and Skworzov[†] prepared α-thujene by the removal of hydrogen chloride from *thujyl chloride* (III) and also by Tschugaev's xanthate method.

The subsequent investigations of Kondakov and Skworzov[‡] and of Tschugaev and Fomin[§] showed the hydrocarbons so



---

[*] *J. Proc. Roy. Soc. New South Wales*, 1938, **71**, 330.

[†] *Chem.-Ztg.* 1902, **26**, 720; *J. pr. Chem.* 1903 [ii], **67**, 574; 1904 [ii], **69**, 176.

[‡] *J. Russ. Phys. Chem. Soc.* 1910, **42**, 497.

[§] *Ber.* 1912, **45**, 1293; compare Henderson and Robertson, *J.C.S.* 1923, **123**, 1715.

obtained to be a mixture of both structural and stereoisomerides. By the decomposition of the liquid methyl xanthate of *d-iso*-thujyl alcohol (see p. 27) at 138°, Tschugaev and Fomin prepared what they considered to be pure *l*-α-thujene.

An inspection of the formula of either thujyl alcohol or of the trimethylammonium hydroxide, the constitutions of which have been rigidly established, shows that, by their decomposition, the formation of two structurally isomeric hydrocarbons (IV) and (V) is theoretically possible. There is no doubt, however, that the higher boiling hydrocarbon, α-thujene, must be represented by formula (IV), since, on oxidation with potassium permanganate, it yields, depending upon the conditions used, either *α-thujaketonic acid* (VI) or *α-thujadicarboxylic acid* (VII).[*] The evidence for the constitution of these two acids is given on p. 36, and it is obvious that the formation of the ketonic acid (VI) definitely establishes the constitution of the hydrocarbon.

α-Thujene has also been obtained by the reduction of sabinol with sodium in liquid ammonia.[†] It is a colourless mobile oil with a somewhat penetrating odour quite different from that of α-pinene. For the natural hydrocarbon Simonsen observed the following constants: b.p. 152–152·5°/699 mm., $d_{30^\circ}^{30^\circ}$ 0·8314, $n_D^{30^\circ}$ 1·4502, $[\alpha]_D^{30^\circ}$ +37·69°, whilst for the synthetic terpene Tschugaev and Fomin quote the values: b.p. 151°/759 mm., $d_{4^\circ}^{20^\circ}$ 0·8301, $n_D^{20^\circ}$ 1·4515, $[\alpha]_D$ −37·20°. It will be observed that the constants for the natural and synthetic hydrocarbons are in good agreement except that the boiling-point of the natural hydrocarbon is about 2° higher.[‡] According to Simonsen, *d*-α-thujene slowly racemises on keeping. It shows complex rotatory dispersion.[§]

α-Thujene can be identified by its low density, by oxidation to *α-thujaketonic acid*, and by its conversion into *terpinene dihydrochloride* by the action of hydrogen chloride. A *nitrosochloride*, m.p. 85–90°, and a 1-*nitrolpiperidide*, m.p. 180°, have been described by Birch.[‖]

---

[*] Wallach, *Annalen*, 1906, **350**, 166; Simonsen, *loc. cit.*; compare Kondakov and Skworzov, *J. pr. Chem.* 1904 [ii], **69**, 181; *J. Russ. Phys. Chem. Soc.* 1910, **42**, 499; Tschugaev, *Ber.* 1904, **37**, 1484.

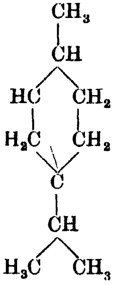
[†] Birch, *J.C.S.* 1945, p. 811.

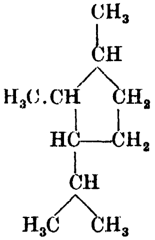
[‡] The natural hydrocarbon contains a small percentage of *d*-α-pinene.

[§] Padmanabhan and Jatkar, *J. Amer. C.S.* 1935, **57**, 334.

[‖] *J. Proc. Roy. Soc. New South Wales*, 1938, **71**, 330; *J.C.S.* 1945, p. 811.

On reduction with hydrogen in the presence of platinum black *l*-α-thujene is converted smoothly into the saturated hydrocarbon, d-*thujane* (VIII) (see p. 5).[*] If, however, the reduction is carried out by the Sabatier-Senderens method with a nickel catalyst, a hydrocarbon, $C_{10}H_{20}$, b.p. 160–161°/740 mm., $d_{4°}^{22°}$ 0·7891, $n_D^{22°}$ 1·4313, is obtained. It is evident that under these conditions fission of the *cyclo*propane ring occurs, since Zelinski and Kasansky[†] have shown that the same hydrocarbon results when α-thujene is distilled over nickel in a current of carbon dioxide, some *p*-cymene being also formed. Kasansky[‡] has shown this hydrocarbon to be 1 : 2-*dimethyl*-3-iso*propyl*cyclo*pentane* (IX).


(VIII)


(IX)

Apart from potassium permanganate, to which reference has already been made, the action of oxidising agents on α-thujene has not been investigated. Rau[§] has shown that the terpene is only very slowly attacked by oxygen and in the presence of a trace of pyrogallol there is no oxidation in five months. According to Tschugaev[‖] it yields with mercuric acetate in acetic acid solution a crystalline derivative.

The *cyclo*propane ring in α-thujene is unstable and readily undergoes fission. By the action of hydrogen chloride or hydrogen bromide in acetic acid solution the corresponding *terpinene dihalogenides* (X) are formed, whilst when shaken for some days with dilute sulphuric acid, a mixture of 1 : 4-*terpin* (XI) and *terpinene*-4-*ol* (XII)[¶] is produced. With boiling 5 per cent.

---

[*] Tschugaev and Fomin, *Compt. rend.* 1910, **151**, 1059.

[†] *Ber.* 1927, **60**, 1096.

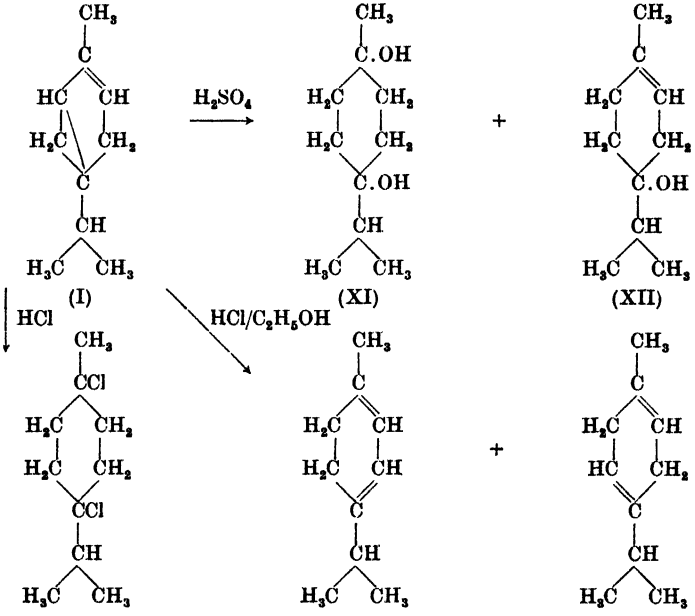
[‡] *Ibid.* 1929, **62**, 2206.

[§] *Ind. For. Rec.* 1924, **11**, 206.

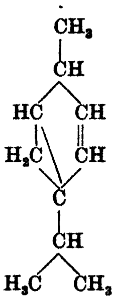
[‖] *Ber.* 1900, **33**, 3121.

[¶] Gascoigne, *J. Proc. Roy. Soc. New South Wales*, 1940, **74**, 359.

ethanolic hydrogen chloride it gives a mixture of α- and γ-terpinenes (XIII) and (XIV).*



β-THUJENE



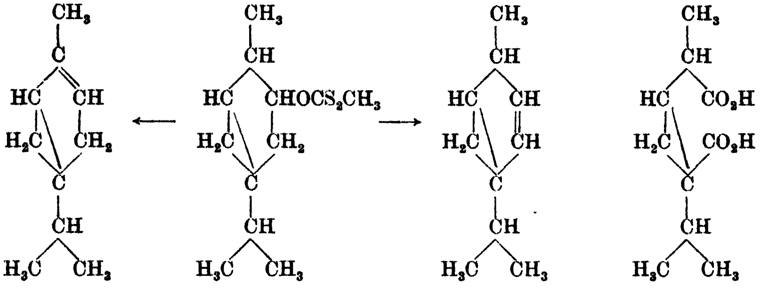
The hydrocarbon, $C_{10}H_{16}$, to which the name β-thujene has been given, was described simultaneously by Tschugaev† and

---

* Wallach, *Annalen*, 1906, **350**, 167; Simonsen, *loc. cit.* p. 298.

† *Ber.* 1904, **37**, 1483.

Kondakov and Skworzov,[*] who prepared it by the distillation of *methyl thujylxanthate* (I). As mentioned on p. 11, *l*-α-thujene (III) is the main product of the reaction, but, as Tschugaev and Fomin[†] found later, *d*-β-thujene (II) is best prepared by the decomposition of the methyl xanthate of *l*-thujyl alcohol (see p. 28) at 183°.


(III) (I) (II) (IV)

According to these authors the hydrocarbon has the following constants, although they do not regard it as absolutely pure and free from α-thujene: b.p. 147°/739 mm., $d_{4°}^{20°}$ 0·8208, $n_D^{20°}$ 1·4470, $[\alpha]_D$ +110·7°, values in close accord with those found by Kondakov and Skworzov[‡] for a specimen purified by treatment with potassium permanganate.

Although at one time β-thujene was considered to be a stereoisomeride of α-thujene, this would appear to be unlikely, in view of the marked difference in their physical properties. The problem of the constitution has been mainly investigated by Kondakov and Skworzov. These authors consider the hydrocarbon to be most probably represented by (II), since on oxidation it yields an optically inactive acid, $C_{10}H_{16}O_4$, m.p. 146°, dl-*homothujadicarboxylic acid* (IV). An optically inactive form of this acid was described by Wallach,[§] who prepared it by the action of sodium hypobromite on thujone. Wallach's acid melted at 179°, but since homothujadicarboxylic acid contains three asymmetric carbon atoms and can exist in *cis-trans*-modifications, the two acids are very probably structurally identical. The constitution of β-thujene cannot, however, be regarded as rigidly established.

---

[*] *J. pr. Chem.* 1903 [ii], **67**, 574; 1904 [ii], **69**, 176.

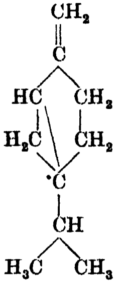
[†] *Ber.* 1912, **45**, 1293.

[‡] *J. Russ. Phys. Chem. Soc.* 1910, **42**, 497.

[§] *Annalen,* 1893, **275**, 180; 1902, **323**, 373; compare Semmler, *Ber.* 1903, **36**, 4367.

The properties of β-thujene have been little studied. On catalytic hydrogenation Tschugaev and Fomin[*] showed that *thujane* was formed identical in all respects with the hydrocarbon prepared from α-thujene. It has been found by Kondakov and Skworzov to be remarkably resistant to oxidation by potassium permanganate, which provides a convenient method for its purification, and they have suggested the possibility that it is tricyclic, but this would appear to be unlikely.

SABINENE



Although Dumas,[†] Levy[‡] and Fromm[§] had observed that oil of savin (from *Juniperis Sabina* L.) appeared to contain a hydrocarbon differing in its properties from pinene, it remained for Semmler[||] to separate the hydrocarbon, to which he gave the name *sabinene*, in a pure state and to determine its constitution.

The hydrocarbon present in oil of savin is dextrorotatory, and this has subsequently been found to be the case with the majority of other oils in which its presence has been established. The laevorotatory form was, however, shown by Simonsen and Rau[¶] to occur in the oil from the seeds of *Zanthoxylum Budrunga* Wall., whilst Penfold and Simonsen[**] have isolated *dl*-sabinene from the oil of the leaves of *Murraya Koenigii* Spreng.

---

[*] *Compt. rend.* 1910, **151**, 1059.

[†] *Annalen*, 1835, **15**, 159.

[‡] *Ber.* 1885, **18**, 3206.

[§] *Ibid.* 1900, **33**, 1192.

[||] *Ibid.* 1900, **33**, 1463.

[¶] *Ind. For. Rec.* 1922, **9**, 141; compare Semmler and Schossberger, *Ber.* 1911, **44**, 2889.

[**] *J. Proc. Roy. Soc. New South Wales*, 1925, **49**, 146.

The constitution of *d*-sabinene (I) was determined by Semmler* in an investigation of the products formed on oxidation with potassium permanganate. When acted upon by this reagent under carefully controlled conditions, the two main products formed are (i) a *glycol*, $C_{10}H_{18}O_2$ (II), and (ii) a *hydroxy acid*, $C_{10}H_{16}O_3$ (VI), whilst an isomeric acid was also separated to which Semmler ascribed formula (X); this cannot, however, be considered as fully established.

The glycol, d-*sabinene glycol*, m.p. 54°, b.p. 148–150°/15 mm., $d^{20°}$ 1·021, n_D 1·402, was dextrorotatory and when warmed with dilute sulphuric acid gave by fission of the *cyclo*propane ring a *dihydrocuminalcohol*, which is probably represented by (III), although no direct evidence of the position of the ethylenic linkages is available.† The relative positions of the *iso*propyl and primary alcohol groups are, however, established by its conversion on controlled oxidation with chromic acid to *cuminalcohol* (IV). The instability of the *cyclo*propane ring in the glycol is further exemplified by its conversion, on treatment with cold dilute sulphuric acid, into the isomeric unsaturated *glycol*, which probably has formula (V). The oxidation of sabinene to a glycol containing a primary alcohol group indicated the presence in the hydrocarbon of an exocyclic ethylenic linkage, a conclusion fully substantiated by the study of the properties of the hydroxy acid, d-*sabinenic acid* (VI). This acid, like the isomeric acid, nopinic acid, derived from β-pinene (see p. 192), can be separated readily by taking advantage of the sparing solubility of its sodium salt.

Sabinenic acid, *d*- and *l*-forms, m.p. 57°, *dl*-, m.p. 84–85°, was, as mentioned above, first prepared by Semmler, a more convenient process for its isolation being described by Wallach.‡ On further oxidation with an acid solution of potassium permanganate or with lead peroxide it gives a ketone, *sabina ketone* (VII), b.p. 218–219°, $d^{20°}$ 0·9555, n_D 1·470, $[\alpha]_D$ −24·41° (*semicarbazone*, m.p. 141°), which is also formed by the direct oxidation of sabinene. On hydrogenation or reduction with sodium and alcohol, sabina ketone gives *d*-α-*sabina ketol*,§ b.p. 100°/16 mm.,

---

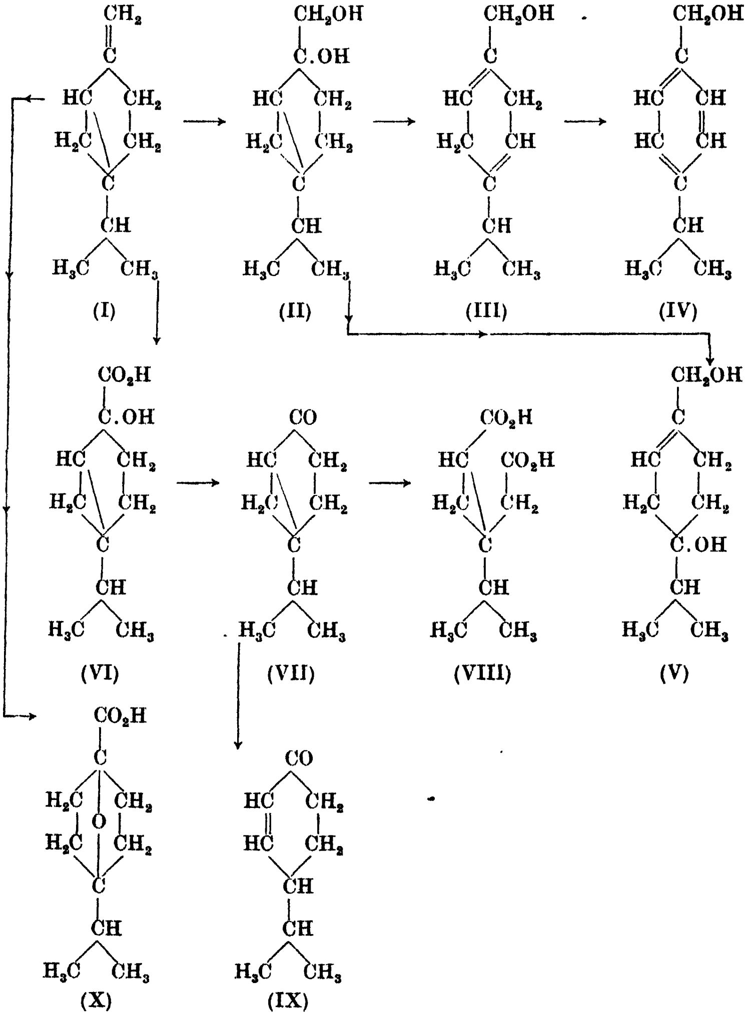
* *Ber.* 1900, **33**, 1463; 1902, **35**, 2047.

† Compare Wallach, *Annalen*, 1906, **345**, 151; 1908, **360**, 95.

‡ *Annalen*, 1908, **359**, 266.

§ Short and Read, *J.C.S.* 1939, p. 1416.

$d_{4^\circ}^{25^\circ}$ 0·9397, $n_D^{25^\circ}$ 1·4670, $\alpha_D^{15^\circ}$ +88·8° (p-*nitrobenzoate,* m.p. 89·5°, $[\alpha]_D^{18^\circ}$ +94° in chloroform; 3:5-*dinitrobenzoate,* m.p. 70°, $[\alpha]_D^{20^\circ}$ +81·5° in chloroform) from which pure *l*-sabina ketone may be obtained by oxidation with chromic acid. The ketone prepared in this way had b.p. 97·5°/17 mm., $d_{4^\circ}^{25^\circ}$ 0·9495, $n_D^{25^\circ}$ 1·4672, $\alpha_D^{16^\circ}$ −19·8°, $[\alpha]_D^{15^\circ}$ −34·2° in alcohol (*semicarbazone,*



m.p. 135–137°, $[\alpha]_D^{15°}$ +137·5° in methanol; 2:4-*dinitrophenylhydrazone*, m.p. 124°, $[\alpha]_D^{15°}$ + 135·2° in chloroform). Amination of sabina ketone with ammonium formate gives *sabina ketylamine*, b.p. 63–64°/19 mm., $n_D^{20°}$ 1·4705, $\alpha_D^{18°}$ +43·8° (*hydrochloride*, m.p. 225°; p-*nitrobenzoyl* derivative, m.p. 141°). Although sabina ketone is stable to potassium permanganate, it is readily isomerised by hot dilute sulphuric acid to 4-iso*propyl*-Δ^2-cyclo*hexenone* (IX), the same ketone being formed when the semicarbazone is hydrolysed with dilute sulphuric acid.[*] On oxidation with sodium hypobromite it yields a dibasic acid, *α-thujadicarboxylic acid* (VIII), identical with the acid obtained by the degradation of α-thujene and thujone (see pp. 12, 36). The formation of this acid establishes beyond question the structure of the *cyclo*propane ring present in sabinene and shows the suggestion of Kondakov and Skworzov,[†] that it is a carane derivative, to be incorrect. The subsequent study of the properties of sabinene have fully confirmed the structure assigned to it by Semmler.

Sabinene has not been prepared synthetically, the method successfully employed in the case of β-pinene (see p. 196) failing owing to the ready fission of the *cyclo*propane ring (see below).

Since sabinene cannot be purified through any crystalline derivative, some variation occurs in the physical constants given in the literature, but the following may be regarded as average values: *d*-sabinene, b.p. 163–165°, $d^{20°}$ 0·842, $n_D^{20°}$ 1·465, $[\alpha]_D$ +80·17°; *l*-sabinene, b.p. 161·5–163°/705 mm., $d_{30°}^{30°}$ 0·8407, $n_D^{30°}$ 1·465, $[\alpha]_D$ −46·19°. As has been remarked by Auwers, Roth and Eisenlohr,[‡] the exaltation of the molecular refraction (+1·34) is one of the highest which has been observed in the terpene group, and it must be ascribed to the conjugation of the exocyclic bond with the *cyclo*propane ring. Padmanabhan and Jatkar[§] have drawn attention to the anomalous rotatory dispersion shown by sabinene. The calorific value is 6179 kg.-cals.

Sabinene can be readily identified by oxidation of the appropriate fraction with potassium permanganate to sabinenic acid.

---

[*] Wallach, *Annalen*, 1908, **359**, 270; 1913, **397**, 208.

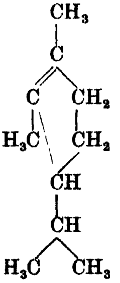
[†] *J. pr. Chem.* 1904 [ii], **69**, 176.

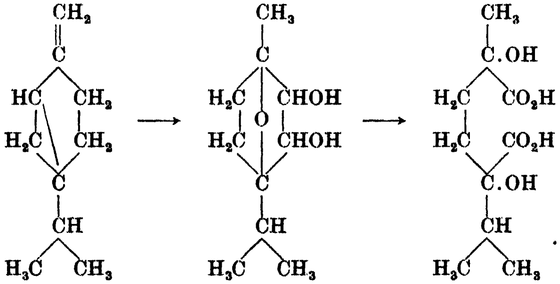
[‡] *Annalen*, 1910, **373**, 275.

[§] *J. Amer. C.S.* 1935, **57**, 334.

The catalytic hydrogenation of the hydrocarbon in the presence of platinum and palladium was investigated simultaneously by Tschugaev and Fomin[*] and by Wallach,[†] who regarded the hydrocarbon obtained as *d*-thujane. A reinvestigation of this reduction by Richter, Wolff and Presting[‡] has shown, however, that whilst in the presence of platinum black *d*-thujane, b.p. 50·4–50·7°/8 mm., $d_{4^\circ}^{18^\circ}$ 0·815, $n_D^{18^\circ}$ 1·409, α_D $+12·4°$, is obtained, when colloidal palladium is the catalyst a more deep-seated change occurs and 1:2-*dimethyl*-3-iso*propyl*cyclo*pentene* is formed. The position of the ethylenic linkage has not been determined, but the hydrocarbon is probably represented by (XI). On further reduction it is converted into 1:2-dimethyl-3-*iso*propyl*cyclo*pentane. The reaction is analogous therefore to that which occurs when *d*-thujane is distilled over palladinised charcoal (see p. 8).

On ozonolysis, as was to be anticipated, sabinene behaves normally and yields sabina ketone (VII).[§] The action of hydrogen peroxide in acetic acid solution on the hydrocarbon has been investigated by Henderson and Robertson,[‖] who have found that two isomeric *glycol anhydrides*, (A) m.p. 174°, $[\alpha]_D$ $+34·3°$ (in alcohol) and (B) m.p. 172°, $[\alpha]_D$ $\pm 0°$, were formed. To these glycols Henderson and Robertson ascribe formula (XII), the oxidation being accompanied by fission of the *cyclo*propane ring. The glycol anhydride (B) gives with hydrogen bromide a *tetrabromide*, m.p. 159–160°, which is probably 1:2:3:4-*tetrabromo*-p-*menthane*.[¶] In order to determine their constitution the two


(XI)


(I) (XII) (XIII)

---

[*] *Compt. rend.* 1910, **151**, 1061.

[†] *Nach. K. Ges. Göttingen*, 1910, p. 544.

[‡] *Ber.* 1931, **64**, 871.

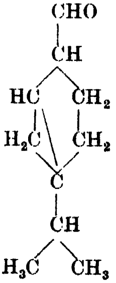
[§] Schmidt, *Z. angew. Chem.* 1929, **42**, 126.

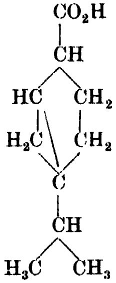
[‖] *J.C.S.* 1923, **123**, 1849.

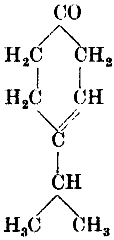
[¶] Henderson and Robertson, *J.C.S.* 1926, p. 2762.

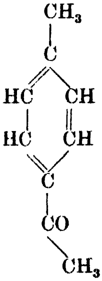
anhydrides were oxidised with potassium permanganate, when the optically active and inactive forms of *αδ-dihydroxy-α-methyl*-δ-iso*propyladipic acid* (XIII) were obtained, which would appear to substantiate the formula assigned to the glycol anhydrides. These two substances are probably stereoisomers of the substance, m.p. 62–64°, prepared by Nelson from ascaridole which, on oxidation with potassium permanganate, gives 1:4-cineolic acid (see Vol. I, p. 449).

By oxidation of sabinene with chromic acid, Treibs and Schmidt[*] obtained a mixture of p-*cymene*, *cuminaldehyde* and 4-iso*propyl*-Δ^2-cyclo*hexenone* (IX). With chromyl chloride, Henderson, Robertson and Brown[†] found the oxidation to proceed in a more complicated manner, to yield a dicyclic aldehyde, *sabinenilanaldehyde*[‡] (XIV), b.p. 215–217° (*semicarbazone*, m.p. 145–149°) which can be oxidised very readily to the corresponding acid, *sabinenilanic acid* (XV), m.p. 175–176°; small quantities of 4-*iso*propyl-Δ^3-*cyclo*hexenone (XVIa) and *p*-tolyl methyl ketone (XVIb) were formed also.


(XIV)


(XV)


(XVIa)


(XVIb)

With bromine, sabinene yields a liquid *dibromide*.[§] Kondakov and Skworzov[||] stated that, by the action of the halogen acids on *d*-sabinene in acetic acid solution, dipentene dihalogenides were formed. This observation was, however, shortly afterwards shown by Wallach[¶] to be incorrect, and that in acetic acid solution the *terpinene dihalogenides* (XVII) are produced. If, however, the reaction is conducted in the absence of a solvent or in carbon disulphide solution, care being taken to exclude all traces of moisture, then a laevorotatory *monohydrochloride* (XVIII), b.p. 82–86°/9 mm., $[\alpha]_D$ $-0{\cdot}5°$, is obtained.[*]

---

[*] *Ber.* 1928, **61**, 459.

[†] *J.C.S.* 1922, **121**, 2717; compare Henderson and Robertson, *ibid.* 1924, **125**, 765.

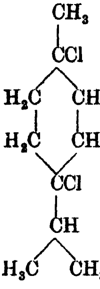
[‡] The authors do not mention if these substances were optically active.

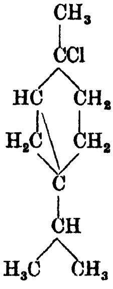
[§] Semmler, *Ber.* 1900, **33**, 1464.

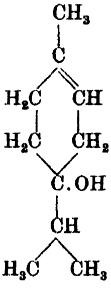
[||] *J. pr. Chem.* 1904 [ii], **69**, 176.

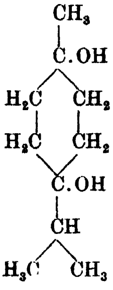
[¶] *Annalen*, 1906, **350**, 164; 1907, **356**, 199.

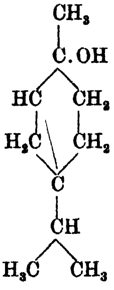
The tendency for sabinene to pass into derivatives of α-terpinene is further exemplified in its reactions with dilute sulphuric acid, which have been investigated by Wallach[†] and which have already been referred to (Vol. I, p. 277). When the hydrocarbon is shaken with dilute sulphuric acid it passes readily into *terpinen-4-ol* (XIX) and 1:4-*terpin* (XX). The conversion into terpinen-4-ol occurs also when the terpene is treated with formic acid.[‡]

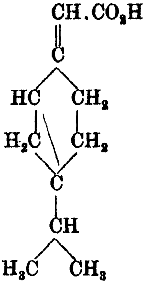

(XVII)


(XVIII)


(XIX)


(XX)


(XXI)


(XXII)

This facile fission of the *cyclo*propane ring is in marked contrast to that observed in the case of the carenes, which do not react with dilute sulphuric acid.

The alcohol, *sabinene hydrate* (XXI), m.p. 38–39°, b.p. 195–201°, which can be prepared by the action of the Grignard reagent on sabina ketone,[§] shows a similar instability and, when shaken with dilute sulphuric acid, gives the same products as the parent hydrocarbon. Sabina ketone condenses apparently normally with ethyl bromoacetate in the presence of zinc to give a hydroxy ester yielding on hydrolysis the unsaturated acid (XXII), m.p. 67–68°.[‖] Although this acid loses carbon dioxide on distillation, it does not yield sabinene, but the monocyclic terpene, β-terpinene (see Vol. I, p. 186).

---

[*] Semmler, *Ber.* 1906, **39**, 4420; 1907, **40**, 754, 2959; Wallach, *Ber.* 1907, **40**, 590; *Annalen*, 1907, **356**, 198.

[†] *Annalen*, 1906, **350**, 165; 1908, **360**, 98. [‡] *Ber.* 1906, **350**, 165; 1908, **360**, 98.

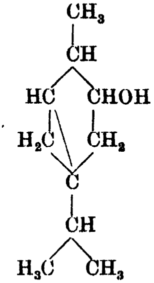
[§] Wallach, *Annalen*, 1907, **357**, 65; 1908, **360**, 94. [‖] *Annalen*, 1908, **362**, 287.

By the condensation of sabinene and isoprene, Semmler and Jonas[*] prepared a monocyclic sesquiterpene, b.p. 129–135°/15 mm., $d^{20°}$ 0·890, n_D 1·5017.

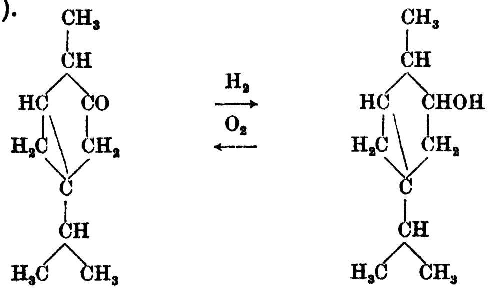
Attention has already been directed (Vol. I, p. 435) to the possible biogenic relationship between sabinene, terpinen-4-ol and 1:4-cineole.

B. ALCOHOLS

THUJYL ALCOHOL



The secondary alcohol, thujyl alcohol, $C_{10}H_{18}O$, known also as tanacetyl alcohol, was found by Schimmel and Co.[†] to be present in the free state and combined with various acids in oil of wormwood (from *Artemisia Absinthium* L.). Prior to its discovery in nature, the alcohol had been prepared simultaneously by Wallach[‡] and by Semmler[§] by the reduction of *thujone* (p. 46) with sodium and alcohol. From its method of preparation and from the fact that on oxidation it can be reconverted into the parent ketone (I), it follows that it must be represented by formula (II).



(I) (II)

---

[*] *Ber.* 1914, **47**, 2081.

[†] *Schimmel's Report*, 1897, April, p. 48.

[‡] *Annalen*, 1892, **272**, 109.

[§] *Ber.* 1892, **25**, 3344.

Inspection of the formula of thujyl alcohol shows that it can exist theoretically in eight optically active and four externally compensated modifications. The natural alcohol, and that prepared by the reduction of thujone, are mixtures of stereoisomerides, which have been investigated by Paolini and his collaborators,* by Tschugaev and Fomin,† and by Short and Read.‡

By the reduction of β-thujone (*d-iso*thujone) from tansy oil, Paolini prepared a thujyl alcohol, b.p. 206–209°, $d^{20°}$ 0·925, $n_D^{20°}$ 1·4635, $[\alpha]_D$ $+69{\cdot}49°$, the hydrogen phthalate of which on fractional crystallisation gave a d-*thujyl hydrogen phthalate*, m.p. 120°, $[\alpha]_D$ $+91{\cdot}27°$. From this by hydrolysis a d-*thujyl alcohol*, b.p. 206°, $d^{16°}$ 0·9229, $n_D^{16°}$ 1·4625, $[\alpha]_D$ $+114{\cdot}6°$, was obtained. An isomeric dextrorotatory alcohol was prepared by Paolini and Divizia by the reduction of α-thujone (*l*-thujone) from thuja oil. From this alcohol a *hydrogen phthalate*, m.p. 95–96°, $[\alpha]_D$ $+2{\cdot}28°$, was obtained and this gave on hydrolysis an alcohol, $[\alpha]_D$ $+50{\cdot}0°$, for which the name δ-*thujyl alcohol* was suggested.

Tschugaev and Fomin, who also used the hydrogen phthalates for the purification of the thujyl alcohol prepared by the reduction of thujone, fractionally crystallised the cinchonine salt. From the sparingly soluble fraction of this salt they obtained an alcohol having $d_{4°}^{20°}$ 0·9187, $[\alpha]_D$ $+116{\cdot}9°$, and Paolini's *d*-thujyl alcohol may contain this as its chief constituent. The hydrogen phthalate regenerated from the soluble cinchonic salt was further purified by crystallisation of the strychnine salt. A second hydrogen phthalate, so obtained, gave on hydrolysis a crystalline l-*thujyl alcohol*, m.p. 28°, $[\alpha]_D$ $-9{\cdot}12°$.

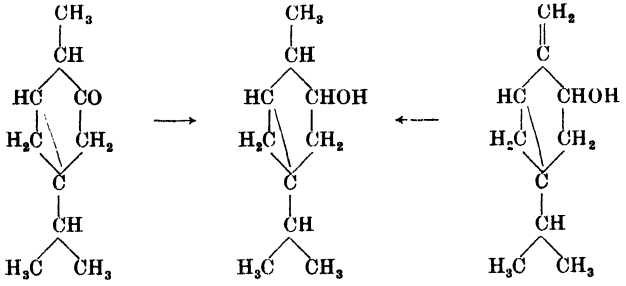
Short and Read have studied the hydrogenation of *l*-thujone (III) and have shown that the main product is l-*thujyl alcohol*, which was obtained in a pure form by repeated crystallisation of the *p*-nitrobenzoate. By reduction of either *l*-thujone or *d-iso*thujone with sodium and alcohol, they have obtained d-iso*thujyl alcohol* (probably identical with the dextrorotatory alcohol of Paolini and of Tschugaev and Fomin), which was purified through the *p*-nitrobenzoate or the 3:5-dinitrobenzoate. A third stereoisomer, l-neo*thujyl alcohol*, was prepared by the hydrogenation of *d*-sabinol (IV) (see p. 31) in the presence of a platinum catalyst,* and it may also be isolated from the reduction products of *l*-thujone. It is probably identical with the crystalline alcohol of Tschugaev and Fomin.

---

* *Atti R. Accad. Lincei*, 1911 [v], **21**, I, 570; *Gazzetta*, 1912, **42**, I, 41.

† *Ber.* 1912, **45**, 1293.

‡ *J.C.S.* 1938, p. 2016; 1939, p. 1040.



(III) (II) (IV)

The properties of these alcohols and of some derivatives are given in the table below:

	m.p.	b.p.	$d_{4°}^{25°}$	n_D	α_D	$[\alpha]_D$ (in ethanol)
l-*Thujyl alcohol*	66–67°	—	—	—	—	−22·5°
l-neo*Thujyl alcohol*	22–23°	96°/13 mm.	0·9223	1·4624/25°	—	− 8·8°
d-iso*Thujyl alcohol*	—	103°/16 mm.	—	1·4630/14°	+108·8	—

	p-*Nitrobenzoate*		3:5-*Dinitrobenzoate*	
	m.p.	$[\alpha]_D$ (in chloroform)	m.p.	$[\alpha]_D$ (in chloroform)
l-*Thujyl alcohol*	101°	− 32·2°	106°	−24·5°
l-neo*Thujyl alcohol*	90°	− 12·5°	103°	−10·0°
d-iso*Thujyl alcohol*	78°	+107°	92°	+96·7°

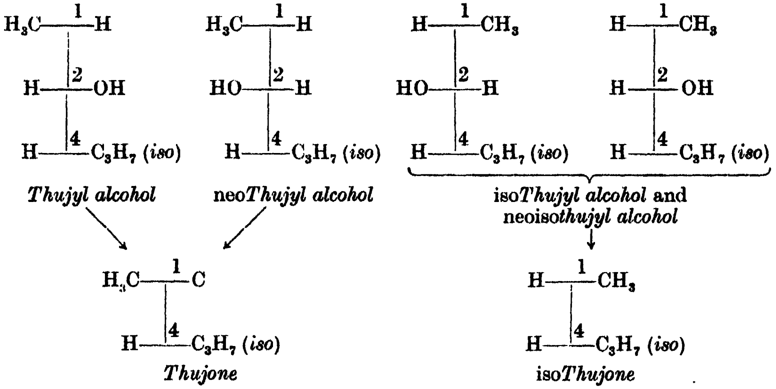
The nomenclature is similar to that adopted in the menthol series (Vol. I, p. 233). Both *l*-thujyl alcohol and *l*-*neo*thujyl alcohol on oxidation with chromic acid give *l*-thujone, whereas *d*-*iso*thujyl alcohol gives *d*-*iso*thujone, which would also be formed from neoiso*thujyl alcohol.* It is not certain whether this alcohol has yet been prepared; it is possibly identical with the δ-thujyl alcohol of Paolini.

Short and Read have shown that *l*-thujyl alcohol reacts more readily than *l*-*neo*thujyl alcohol with *p*-nitrobenzoyl chloride.

---

* Compare Semmler, *Ber.* 1900, **33**, 1461; Wallach, *Nach. Ges. Wiss. Gött.* 1919, **3**, 321; Henderson and Robertson, *J.C.S.* 1923, **123**, 1715.

From analogy with similar considerations in the menthol series the latter is therefore considered to be the *cis-* form. Assuming that *l*-thujone has a *trans*-configuration, since it has a lower refractive index and density than *d-iso*thujone, the various alcohols and ketones may be represented as shown below, although it must be emphasised that in the absence of further evidence the configurations cannot be regarded as finally established.



Thujyl alcohol[*] is a colourless substance with an odour resembling that of carvomenthol. Owing to the presence of the *cyclo*propane ring the molecular refraction shows a marked exaltation (+0·62). The calorific value determined by Roth and Ostling[†] is 1479·4 kg.-cals. and is higher than that of borneol.

The alcohol can be identified readily by oxidation to thujone and the preparation of the characteristic derivatives of the ketone.

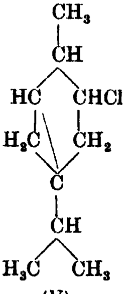
Thujyl alcohol shows considerable stability and unlike thujone it does not isomerise when heated. With the halogens it does not yield any characteristic derivatives, whilst with the halogen acids the reactions taking place would appear to be somewhat complex. By the action of hydrogen chloride in acetic acid solution or with phosphorus pentachloride in light petroleum, *thujyl chloride* is obtained.[‡] This chloride, which boils over a wide range, 72–82°/10 mm., is not homogeneous and is a mixture of thujyl chloride (V) and monocyclic chlorides formed by the fission of the *cyclo*propane in either of the two directions indicated by the partial formulae (VI) and (VII). The presence of thujyl chloride in the mixture was proved by Kondakov and Skworzov,[*] who showed that on treatment with alkali a mixture of α- and β-thujenes was obtained.

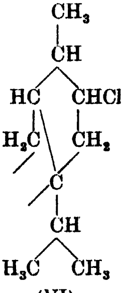
---

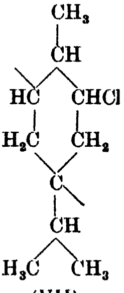
[*] Unless specified, this term may be taken to refer to a mixture of stereoisomerides.

[†] *Ber.* 1913, **46**, 323.

[‡] Semmler, *Ber.* 1892, **25**, 3345; Kondakov, *J. pr. Chem.* 1900 [ii], **62**, 176.


(V)


(VI)


(VII)

With hydrogen bromide in acetic acid solution[†] a mixture of *bromides* is obtained, b.p. 100–128°/11 mm., which apparently does not contain any thujyl bromide, since treatment with alkali gives a mixture of monocyclic alcohols, $C_{10}H_{18}O$, b.p. 218–225°, the nature of which has not been determined. Although thujyl alcohol is decomposed on warming with dilute sulphuric acid, it is stable in the cold and differs in this respect from sabinol[‡] (compare p. 32).

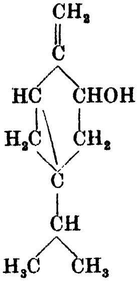
A number of esters of thujyl alcohol have been described, but esterification does not take place smoothly owing to the tendency for hydrocarbon formation to occur simultaneously. Of particular interest are the *methyl thujylxanthates*, $C_{10}H_{17}O.CS_2.CH_3$, first prepared by Tschugaev[§] and subsequently investigated more thoroughly by Tschugaev and Fomin.[||] When prepared from ordinary thujyl alcohol these esters are oils, which decompose on heating, yielding a mixture of α- and β-thujenes. The ester prepared, however, from *d-iso*thujyl alcohol decomposes at 138° with formation of pure *l*-α-thujene; that from *l-neo*thujyl alcohol is more stable and only decomposes at 183° to give mainly *d*-*β*-thujene.

---

[*] *J. pr. Chem.* 1904 [ii], **69**, 176.
[†] Kondakov, *Chem.-Ztg.* 1902, **26**, 723.
[‡] Wallach, *Annalen*, 1895, **286**, 109; 1908, **360**, 93.
[§] *Ber.* 1900, **33**, 3120.
[||] *Ibid.* 1912, **45**, 1293.

Attention may be directed finally to the interesting investigations of Charabot* on the oil content of the French *A. Absinthium* at different periods in the growth of the herb and the relative proportions of thujyl alcohol (or thujyl esters) and thujone present. A parallel investigation on the American herb has been made by Rabak.†

SABINOL



d-Sabinol, $C_{10}H_{16}O$, occurs in nature, both free and in the form of its acetate, in oil of savin (from *Juniperis Sabina* L.).‡

d-Sabinol was first investigated by Fromm, who showed that it was an unsaturated alcohol, $C_{10}H_{16}O$, which on oxidation with potassium permanganate gave *α-thujadicarboxylic acid* (III) and contained therefore the dicyclic structure of the hydrocarbon, sabinene. At the time of these experiments the constitution of α-thujadicarboxylic acid was not known. A more comprehensive study of the oxidation products of *d*-sabinol was made by Semmler,§ and he was able to show that the alcohol must have formula (I). By the action of cold dilute potassium permanganate a trihydroxy alcohol, *sabina glycerol* (II), m.p. 152–153°, is formed, which, when shaken with dilute sulphuric acid, is converted into an unsaturated glycerol, probably Δ^1-p-*menthene*-4:6:7-*triol* (IV),‖ whilst, when it is warmed with the same reagent, it yields *cuminalcohol* (V). It will be observed that the conversion of sabina glycerol into the primary alcohol definitely proves the presence of an exocyclic ethylenic linkage in sabinol. The further oxidation of the glycerol with potassium permanganate leads to the cyclic acid, α-thujadicarboxylic acid (III), the determination of the constitution of which is discussed on pp. 36, 37.

---

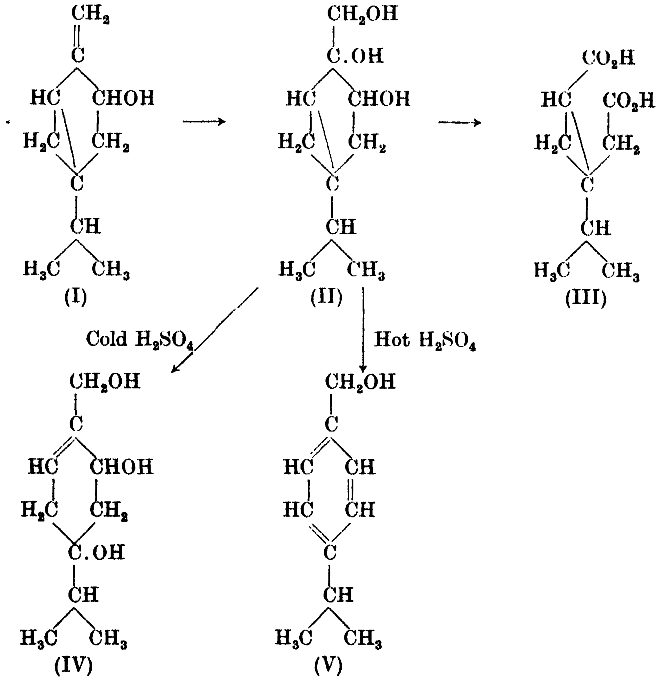
* *Bull. Soc. chim.* 1900 [iii], **23**. 474; *Compt. rend.* 1900, **130**, 923.

† *Ind. Eng. Chem.* 1921, **13**, 536.

‡ *Schimmel's Report*, 1895, **2**, 44; Fromm and Lischke, *Ber.* 1898, **31**, 2025.

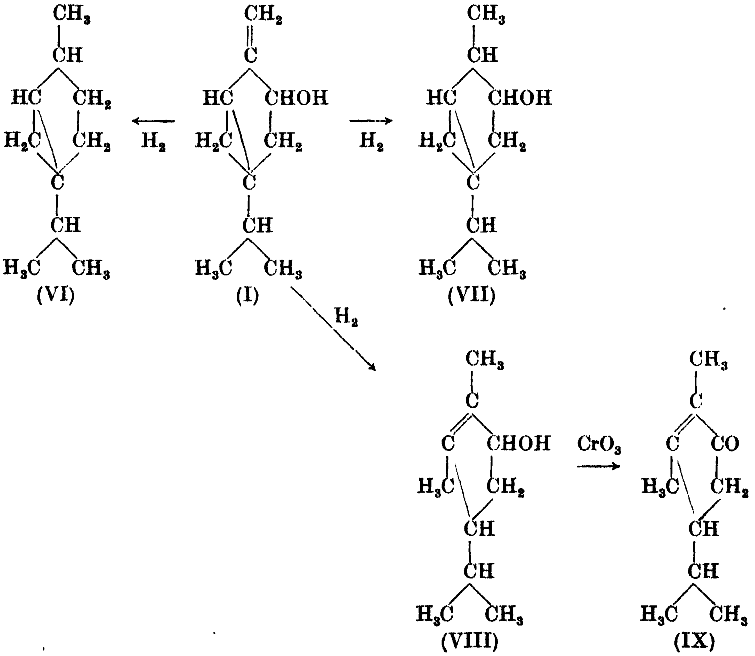
§ *Ber.* 1900, **33**, 1460; compare Fromm, *ibid.* 1193.

‖ Wallach, *Annalen*, 1908, **360**, 96.



d-Sabinol is an oil, which, after purification through its crystalline hydrogen phthalate (see below), has b.p. 208°, $d^{15°}$ 0·9518, $n_D^{18°}$ 1·4895, $[\alpha]_D$ + 7·56°; like the parent hydrocarbon (see p. 19) it shows a marked molecular exaltation of the refractive index (+ 1·5). The alcohol can be characterised by the preparation of the p-*nitrobenzoate*, m.p. 75°, the 3:5-*dinitrobenzoate*, m.p. 109°, or by oxidation to α-thujadicarboxylic acid.

Since sabinol contains three asymmetric carbon atoms, it can theoretically exist in eight optically active forms, but owing to the presence of the *cyclo*propane ring it is unlikely that more than four forms would be stable. The alcohol from oil of savin was considered by Paolini and Rebora[*] to be homogeneous; they obtained a crystalline *hydrogen phthalate*, m.p. 94–95°, $[\alpha]_D$ $-14{\cdot}63°$ (in methyl alcohol). Short and Read,[†] however, have found this derivative to have m.p. 101–102°, $[\alpha]_D^{17°}$ $-17{\cdot}5°$ in methanol, $[\alpha]_D^{17°}$ $+10{\cdot}0°$ in chloroform. No other forms of the alcohol have been described.



(VI) (I) (VII)

(VIII) (IX)

The catalytic hydrogenation of *d*-sabinol has been investigated by Wallach[‡] and by Henderson and Robertson,[§] and by Short and Read.[‖] With a nickel catalyst at 170–175°, it yields a mixture of hydrocarbons from which *thujane* (VI) and a *hydrocarbon*, b.p. 161–163°/763 mm., $d^{20°}$ 0·7950, n_D 1·4300, were separated. Although the constitution of the latter was not determined, it seems not improbable that it is identical with the *cyclo*pentane hydrocarbon which has been obtained both by the reduction of α-thujene and thujone (see pp. 13, 46). Using a platinum catalyst at the ordinary temperature, the main product of the hydrogenation is the saturated alcohol, *dihydrosabinol* (VII), b.p. 206–208°, $d^{20°}$ 0·9160, n_D 1·4601, which is *laevo*-rotatory; at the same time some thujane is also formed together with the hydrocarbon of unknown constitution referred to above. Dihydrosabinol is identical with thujyl alcohol, and as prepared above consists mainly of l-neo*thujyl alcohol*, m.p. 23° (see p. 25). Thujyl alcohol is also produced by the reduction of sabinol with sodium in alcoholic solution.[*] With a palladium catalyst, fission of the *cyclo*propane ring occurs to a considerable extent, and the products contain in addition to thujyl alcohol and hydrocarbons, a quantity of d-2:3-*dimethyl*-4-iso*propyl*-Δ^2-cyclo*pentenol* (VIII), b.p. 90–91°/10 mm., $n_D^{20°}$ 1·4670, $\alpha_D^{19°}$ +28·2° (p-*nitrobenzoate*, m.p. 46·5°, 3:5-*dinitrobenzoate*, m.p. 63–64°), which on oxidation gives d-2:3-*dimethyl*-4-iso*propyl*-Δ^2-cyclo*pentenone* (IX); this ketone is identical with the so-called "Isothujon" obtained by the isomerisation of thujone with sulphuric acid (see p. 39). By reduction of *d*-sabinol with sodium in liquid ammonia *l*-α-thujene is obtained.[†]

---

[*] *Atti R. Accad. Lincei*, 1916 [v], **25**, II, 377.

[†] *J.C.S.* 1939, p. 1040.

[‡] *Nach. Ges. Wiss. Gött.* 1919, **3**, 321.

[§] *J.C.S.* 1923, **123**, 1715.

[‖] *Loc. cit.*

According to Semmler, sabinol undergoes a somewhat remarkable reaction when heated with zinc dust, being isomerised to thujone. Treibs and Schmidt[‡] have found that, when sabinol is distilled over nickel or copper, a mixture of α- and β-thujones together with a little carvotanacetone is obtained. The conversion of *d*-sabinol into thujone, accompanied by some "Isothujon", also occurs when the alcohol is heated with aluminium *iso*propoxide at 160° or with sodium hydroxide,[§] so that the tendency for sabinol to isomerise to thujone is evidently considerable.

The oxidation of *d*-sabinol with ozone has been investigated by Hasselström,[‖] who has shown that formaldehyde, α-thujadicarboxylic acid (III) and the *semi-aldehyde* (XI) of this acid are produced. In addition, an oxide was separated which probably has formula (X), since, on treatment with an alcoholic solution of potassium hydroxide, it gives (XI).

On oxidation with hydrogen peroxide in acetic acid solution, *d*-sabinol gives the two isomeric glycol anhydrides which are obtained when *d*-sabinene is treated with this reagent (see p. 20).[*] With chromic acid it gives the same oxidation products as sabinene (p. 21).

---

[*] Semmler, *Ber.* 1900, **33**, 1461.

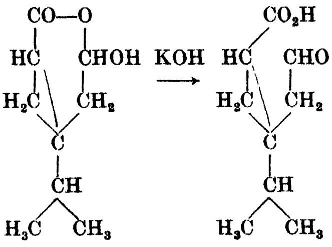
[†] Birch, *J.C.S.* 1945, p. 812.

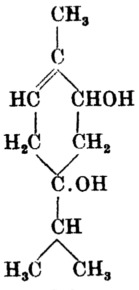
[‡] *Ber.* 1927, **60**, 2340.

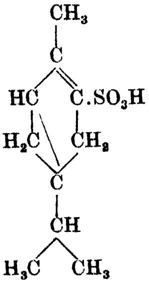
[§] Schmidt, *Ber.* 1929, **62**, 105.

[‖] *Annal. Acad. Sci. Fennicae*, 1927, A **29**, no. 5, 3.

With bromine, *d*-sabinol does not give any characteristic derivatives, whilst the halogen acids cause ring fission and dehydrogenation to *p*-cymene.[†] Ring fission also occurs when the alcohol is shaken with dilute sulphuric acid (5 per cent.), Δ^1-p-*menthene*-4:6-*diol* (XII) being formed.[‡] By the action of sulphur dioxide on an alcoholic solution of *d*-sabinol, Wallach[§] prepared an interesting derivative, m.p. 98–99°, which he suggests is probably the *sulphonic acid* (XIII), since, on hydrolysis with alkali, it yields an unsaturated alcohol, which on reduction and oxidation gives thujone.

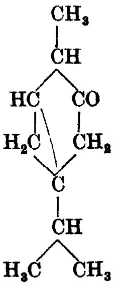

(X) (XI)


(XII)


(XIII)

C. KETONES

THUJONE



---

[*] Henderson and Robertson, *J.C.S.* 1926, p. 2761.

[†] Fromm, *Ber.* 1898, 31, 2030; 1900, 33, 1208.

[‡] Wallach, *Annalen*, 1908, 360, 99.

[§] *Nach. Ges. Wiss. Gött.* 1919, 3, 321.

The ketone, thujone, $C_{10}H_{16}O$, is found fairly widely distributed in nature, occurring, *inter al.*, in thuja oil (from *Thuja occidentalis*), sage oil (*Salvia officinalis* L.), tansy oil (*Tanacetum vulgare* L.) and wormwood oil (*Artemisia absinthium* L.).

In 1878 Bruylants[*] prepared from tansy oil a crystalline bisulphite compound from which he regenerated, by the action of alkali, a substance of the formula $C_{10}H_{16}O$, which he considered to be an aldehyde, whilst at about the same time Muir and Sugiura[†] isolated from sage oil a body of this composition, to which they gave the name *salvinol*. A few years later Jahns[‡] showed that the higher boiling fraction of thuja oil could be separated into two fractions: (i) b.p. 195–197°, $[\alpha]_D$ $-8{\cdot}28°$ and (ii) b.p. 197–199°, $[\alpha]_D$ $+7{\cdot}21°$. In a reinvestigation of this oil Wallach[§] found the low boiling laevorotatory fraction to consist of *l*-fenchone, whilst the high boiling dextrorotatory fraction contained a new ketone, for which he suggested the name *thujone*. On oxidation with potassium permanganate, this ketone gave two isomeric ketonic acids, α- and *β-thujaketonic acids*, $C_{10}H_{16}O_3$. Simultaneously, Semmler[‖] was investigating tansy oil, and he found that the substance isolated by Bruylants was not an aldehyde, but a saturated ketone, $C_{10}H_{16}O$. This ketone, which he designated tanacetone, was characterised by the preparation of an oxime, m.p. 51·5°, and by oxidation with potassium permanganate to a *ketonic acid*, $C_{10}H_{16}O_3$, and a *dicarboxylic acid*, $C_9H_{14}O_4$. Semmler made the further very important observation that the ketones present in thuja, sage, tansy and wormwood oils were apparently all structurally identical, since, on oxidation, they all gave the same dicarboxylic acid, *α-thujadicarboxylic acid* or *α-tanacetonedicarboxylic acid*, m.p. 142°, having the same rotatory power. He pointed out, however, that, although these ketones appeared to be structurally identical, they had not the same properties. All specimens of the ketone did not yield crystalline bisulphite compounds or crystalline oximes, whilst they showed marked differences in their optical rotatory power. He suggested the possibility that the difference in properties was due to the ketones being mixtures of stereoisomerides. He suggested further that the dextrorotatory ketone from tansy oil should be called *tanacetone* or *β-thujone,* and that prepared from thuja oil, which was laevorotatory, *α-thujone.*

---

[*] *Ber.* 1878, **11**, 449.

[†] *Year Book of Pharm.* 1877, p. 498; *J.C.S.* 1880, **37**, 678.

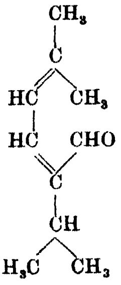
[‡] *Arch. Pharm.* 1883, **221**, 748.

[§] *Annalen*, 1893, **272**, 99.

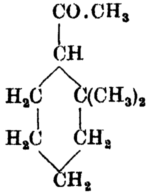
[‖] *Ber.* 1892, **25**, 3343.

Owing to its tendency to isomerise, the determination of the constitution of thujone involved considerable difficulties and it was only established after a prolonged series of investigations in which Semmler, Tiemann and Wallach participated.

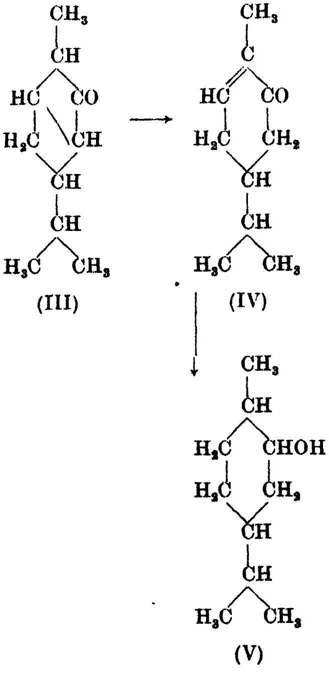
As mentioned above, Bruylants considered thujone to be an aldehyde and suggested the constitution represented by (I) which was disproved when Wallach and Semmler found it to be a ketone. From the ease with which it was attacked by potassium permanganate, Wallach was led to conclude that it was an unsaturated cyclic ketone; he did not, however, determine the constitution of either of the isomeric ketonic acids obtained on oxidation, although he showed that on heating they both gave an unsaturated acyclic *ketone,* $C_7H_{12}.CO.CH_3$.



(I)



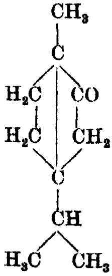
(II)



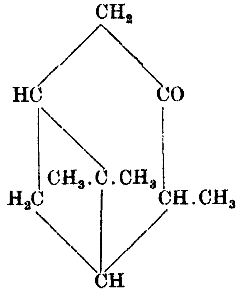
(III) (IV)

(V)

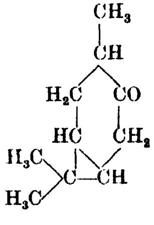
From his experiments, however, Semmler concluded that it was a saturated dicyclic ketone. He found that it was oxidised slowly by sodium hypobromite to give an acid, $C_9H_{14}O_2$, a reaction which appeared to show the presence of the group —CO.CH_3. To explain this result and also to account for the formation of the two isomeric ketonic acids, $C_{10}H_{16}O_3$, which he considered to be stereoisomerides, Semmler suggested formula (II). Two years later, however,[*] he replaced this by (III) to account for the fact that thujone was readily isomerised when heated to yield the monocyclic unsaturated ketone, *carvotanacetone* (IV), which could be reduced to *carvomenthol* (V). Although the relative positions of the methyl, *iso*propyl and carbonyl groups were correctly allocated—for as Wallach[†] showed, thujone could be converted into carvacrol—this formula became untenable when Wallach prepared a *hydroxymethylene* derivative, thus proving the presence of the group —CH_2.CO—. Wallach tentatively suggested (VI), a representation which had at one time been assigned to camphor. It was, however, difficult to explain how a substance having this formula could on oxidation give a ketonic acid containing the group —CO.CH_3. Other formulae, (VII) and (VIII), were suggested by Wagner[‡] and by Kondakov,[§] the latter being based on the erroneous observation that α- and β-thujenes give with hydrogen chloride dipentene dihydrochloride.



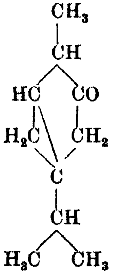
(VI)



(VII)



(VIII)



(IX)

In 1900 Semmler[||] advanced a formula (IX), which is now accepted as correct. This was based on the determination of the constitution of the two thujaketonic acids and on that of the isomeric ketone, "*Isothujon*", which can be prepared by the isomerisation of thujone (see below).

---

[*] *Ber.* **1894**, **27**, 895.

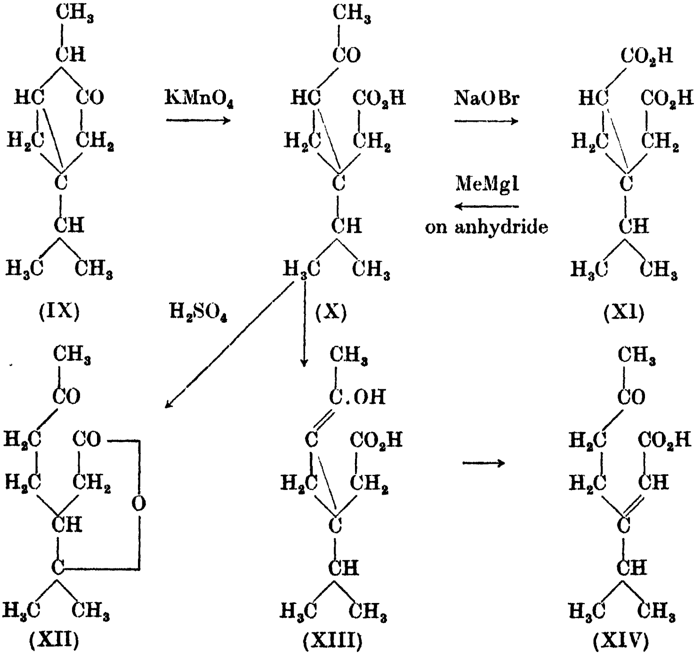
[†] *Ibid.* **1895**, **28**, 33.

[‡] *Ibid.* **1896**, **29**, 885.

[§] *Chem.-Ztg.* 1902, **26**, 720.

[||] *Ber.* **1900**, **33**, 275.

Although in his earlier experiments, to which reference was made above, Wallach had found that the oxidation of thujone with potassium permanganate resulted in the formation of both α- and β-thujaketonic acids, the later experiments of Tiemann and Semmler[*] showed that, if the oxidation was carried out in dilute solution at a low temperature, only α-thujaketonic acid, m.p. 75–76°, $[\alpha]_D$ +192° (in ether), *oxime*, m.p. 174–176°,[†] *semicarbazone*, m.p. 182–183°,[‡] 197°,[§] was obtained in an almost quantitative yield. Although the constitution of this acid has not been established by its direct synthesis, there can be no doubt that it is the *cyclo*propane acid (X). On oxidation with sodium hypobromite, it gives a stable dicarboxylic acid, d-α-



---

[*] *Ber.* 1897, **30**, 431.

[†] Thomson, *J.C.S.* 1910, **97**, 1511.

[‡] Wallach, *Ber.* 1897, **30**, 426.

[§] Seyler, *Ber.* 1902, **35**, 550; Simonsen, *Ind. For. Rec.* 1922, **9**, 293.

thujadicarboxylic acid (XI), m.p. 141–142°, $[\alpha]_D$ +171·5° (in chloroform solution), which yields an *anhydride*, m.p. 55–56°.

Guha and Muthanna* have succeeded in reconverting this anhydride into the ketonic acid (X) by treatment with methyl magnesium iodide, and have also succeeded in synthesising the dicarboxylic acid (XI) from umbellularic acid (see p. 57); since the latter acid had already been synthesised (p. 56), this amounts to a total synthesis of α-thujaketonic acid. When the ketonic acid is warmed with dilute sulphuric acid, fission of the *cyclo*propane ring is accompanied by isomerisation, with the formation of the keto-lactone, *homoterpenyl methyl ketone*, $C_{10}H_{16}O_3$ (XII), m.p. 63°,† which can be prepared also from α-terpineol (Vol. I, p. 259), whilst, on distillation under diminished pressure or on digestion with water, it is converted into an unsaturated acid, *β-thujaketonic acid*, which crystallises in needles, m.p. 78–79° (*oxime*, m.p. 111–112°, *semicarbazone*, m.p. 195–196°); as will be shown, this must have formula (XIV).

If the formula of α-thujaketonic acid be inspected, it will be observed that the *enolic* form (XIII) has an ethylenic linkage attached to the *cyclo*propane ring. As is well known, this structure is unstable, and it is probably due to the intermediate formation of this substance that the α-ketonic acid owes its tendency to isomerise, since the dicarboxylic acid (XI) is stable.

When β-thujaketonic acid is heated at the ordinary pressure it loses carbon dioxide with formation of the unsaturated ketone, $C_9H_{16}O$, *thuja ketone* (2-*methyl*-3-*methyleneheptan*-6-*one*), b.p. 184–186°, $d^{20°}$ 0·854, $n_D^{20°}$ 1·4410. For this ketone Wallach‡ suggested formula (XV), since it passed readily into a hydrocarbon which, from its reactions, was undoubtedly *dihydro-ψ-cumene* (XVI). More direct evidence of the constitution of this ketone was furnished by Tiemann and Semmler,§ who showed that, on oxidation with potassium permanganate, it gave a *glycol*, $C_9H_{18}O_3$ (XVII), which on distillation under diminished pressure passed with loss of water into the *dioxide* (XVIII). Some further reactions of the ketone have been described by Werner and Bogert.‖

---

* *Ber.* 1938, **71**, 2668, 2771; *J. Ind. Inst. Sci.* 1939, **22** A, 278.

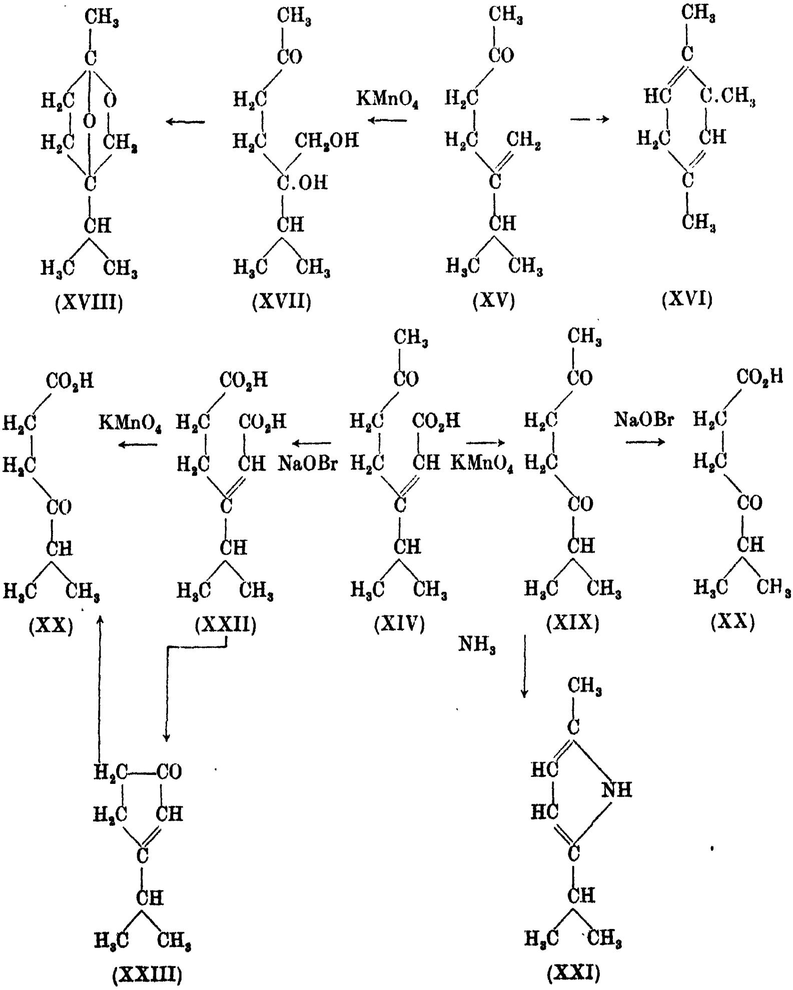
† Tiemann and Semmler, *Ber.* 1896, **29**, 543.

‡ *Annalen*, 1893, **275**, 174.

§ *Ber.* 1897, **30**, 440.

‖ *J. Org. Chem.* 1939, **3**, 578.

When β-thujaketonic acid (XIV) is oxidised with potassium permanganate it yields a diketone, which must be *ω-dimethyl acetonylacetone* (XIX), since, on oxidation with sodium hypobromite, it gives *ω-dimethyl-levulinic acid* (XX) and with alcoholic ammonia 1-*methyl*-4-iso*propylpyrrole* (XXI), the latter reaction being characteristic of 1:4-diketones. Oxidation of β-thujaketonic acid with sodium hypobromite was shown by Tiemann



and Semmler, and also by Wallach, to give a dibasic acid, *β-thujadicarboxylic acid* (XXII), m.p. 116–118°, the constitution of which was definitely established by its oxidation to *ω-dimethyllevulinic acid* (XX). Further evidence[*] in support of the formula assigned to β-thujadicarboxylic acid was supplied by the conversion of its calcium salt on distillation into the cyclic unsaturated ketone, *tanacetophorone* (XXIII), b.p. 212–214°, $d^{20°}$ 0·938, $n_D^{20°}$ 1·4788 (*semicarbazone*, m.p. 187–188°), which on oxidation with potassium permanganate gives the substituted levulinic acid (XX). According to Ranta,[†] when a 4 per cent. solution of β-thujadicarboxylic acid is heated it is partly converted into an *isomeric acid*, m.p. 155–156°, which is probably a stereoisomer, since on oxidation it gives the same products as the original acid.

Whilst the experiments outlined above elucidated the constitution of α- and β-thujaketonic acids and the related dicarboxylic acids, and so established beyond question the presence of a *cyclo*propane ring in thujone, direct evidence of the associated *cyclo*pentane ring was furnished by a study of the ketone "*Isothujon*".[‡] It was observed by Baeyer[§] that, when thujone was dissolved in concentrated sulphuric acid, isomerisation occurred with the formation of a ketone, which gave with an alcoholic solution of potassium hydroxide a cherry red colour. The most satisfactory conditions for effecting the isomerisation were determined later by Wallach[‖] and by Haller,[¶] who found the reaction to proceed most readily when thujone was dissolved in about three times its volume of cold sulphuric acid. The experiments now to be discussed were carried out with "Isothujon" prepared in this manner although, as Wallach[**] pointed out, the ketone is always a mixture of "Isothujon", thujone and carvotanacetone, and can only be purified with great difficulty through its semicarbazone.

---

[*] Semmler, *Ber.* 1892, **25**, 3350; 1897, **30**, 439; Wallach, *Annalen*, 1911, **381**, 85.

[†] *Chem. Zentr.* 1938, II, 2122.

[‡] In the following discussion, the term "Isothujon" has been used rather than the English equivalent "*iso*thujone", since the latter is now applied to the *cis*-isomer of thujone. Compare Short and Read, *J.C.S.* 1939, p. 1040, who have suggested that "Isothujon" should in future be given its systematic name, 2:3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone. The corresponding hydrocarbon is sometimes termed "Isothujan".

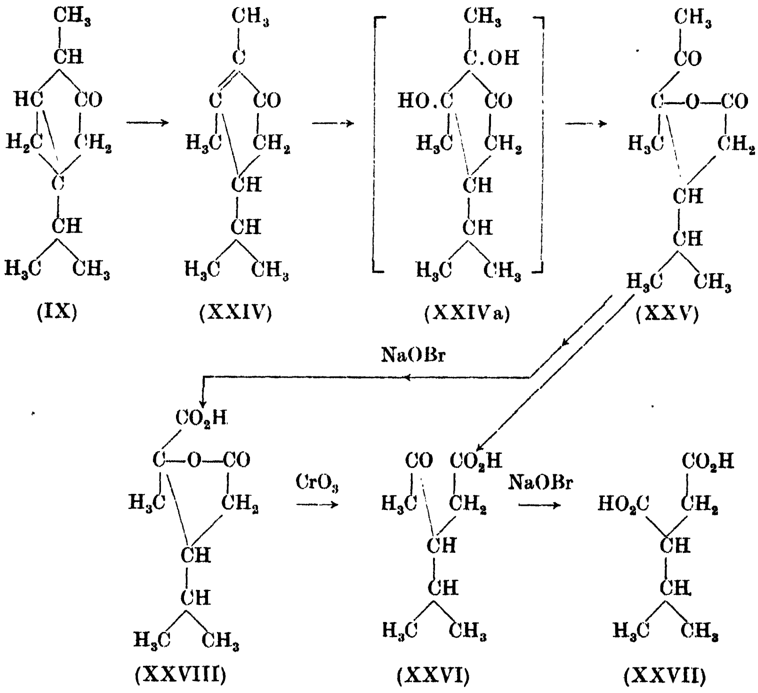
[§] *Ber.* 1894, **27**, 1922.

[‖] *Annalen*, 1895, **286**, 101; 1902, **323**, 334; *Ber.* 1895, **28**, 1958.

[¶] *Compt. rend.* 1905, **140**, 1630.

[**] *Annalen*, 1915, **408**, 163.

When "Isothujon", b.p. 231–232°, d^{20° 0·927, $n_D^{20^\circ}$ 1·4821,[*] is oxidised with potassium permanganate[†] it yields a substance $C_{10}H_{16}O_3$, m.p. 43°, b.p. 273°, which has been found to be a *ketolactone* and must be represented by (XXV), since, on further oxidation, it gives *β*-iso*propyl-levulinic acid* (XXVI), the constitution of which is proved by its degradation with sodium hypobromite to iso*propylsuccinic acid* (XXVII). The ketolactone is only very slowly attacked by potassium permanganate, when an *acid* $C_9H_{14}O_4$, m.p. 52–53°, is formed, which can be prepared more readily by its oxidation with either sodium hypobromite or dilute nitric acid. This acid is undoubtedly the *lactonic acid*



(IX) (XXIV) (XXIVa) (XXV)

(XXVIII) (XXVI) (XXVII)

---

[*] Compare Auwers and Eisenlohr, *J. pr. Chem.* 1910 [ii], **82**, 155.

[†] Wallach, *Ber.* 1897, **30**, 426; *Annalen*, 1902, **323**, 335; Semmler, *Ber.* 1900, **33**, 276.

(XXVIII), since it is oxidised by chromic acid to *β*-iso*propyl-levulinic acid* (XXVI). All these reactions can be readily explained if "Isothujon" is 2:3-*dimethyl*-4-iso*propyl*-Δ^2-cyclo*pentenone* (XXIV), the primary product (XXIVa) of its oxidation passing into the ketolactone.

Confirmatory evidence of the constitution of "Isothujon" was obtained by a study of its reduction products. When reduced with sodium and alcohol,* it yields *α-thujamenthol* (XXIX), b.p. 211–212°, $d^{20°}$ 0·9015, $n_D^{20°}$ 1·4630, from which, by oxidation with chromic acid, the corresponding saturated ketone, *α-thujamenthone* (XXX), b.p. 209–209·5°, $d^{18°}$ 0·8915, $n_D^{20°}$ 1·4474 (*oxime*, m.p. 97°, *semicarbazone*, m.p. 185°), can be prepared.

A stereoisomeric ketone, *β-thujamenthone*, b.p. 215–216°, $d^{19°}$ 0·8890, $n_D^{19°}$ 1·4511 (*oxime*, m.p. 130–131°, *semicarbazone*, m.p. 190–191°), is obtained when "Isothujon" is hydrogenated catalytically in the presence of palladium.† It will be observed that the two isomerides show a very marked difference in their physical properties, but there can be no doubt that they are stereo- and not structural isomers, since they both yield the same oxidation products. This difference is shown also by the alcohol, *β-thujamenthol*, b.p. 216·5–217·5°, $d^{19°}$ 0·8995, $n_D^{20°}$ 1·4583, which can be prepared from the ketone by reduction with sodium and alcohol. When either α- or β-thujamenthones are oxidised with chromic acid, a *ketonic acid*, $C_{10}H_{18}O_3$, b.p. 150–170°/10 mm. (*semicarbazone*, m.p. 174–175°) is obtained, which must be represented by (XXXI), since it gives with sodium hypobromite *α-methyl-β*-iso*propylglutaric acid*, m.p. 137–138° (XXXII). An additional product of the oxidation of the thujamenthones is the *ketolactone*, $C_{10}H_{16}O_3$, m.p. 43° (XXV), identical with that formed by the oxidation of "Isothujon".

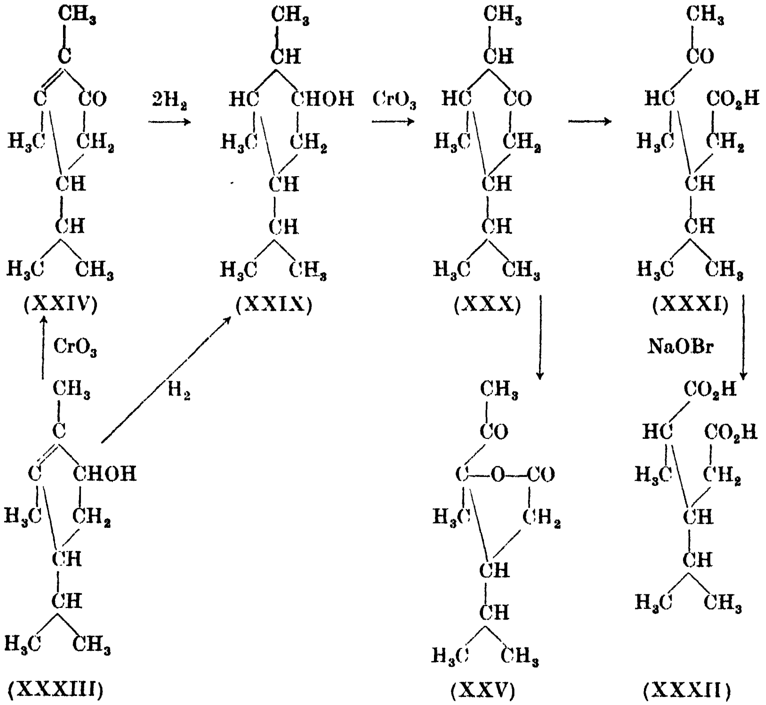
It has already been mentioned (p. 31) that "Isothujon" has also been obtained by oxidation of 2:3-*dimethyl*-4-iso*propyl*-Δ^2-cyclo*pentenol* (XXXIII), a reduction product of sabinol. The ketone obtained by this method had b.p. 89°/13 mm., $n_D^{19°}$ 1·4641,‡ $\alpha_D^{18°}$ −12·7° (*semicarbazone*, m.p. 155–156°, 2:4-*dinitrophenyl-*

---

* Wallach, *Annalen*, 1895, **286**, 104; 1902, **323**, 352; 1903, **329**, 127.

† *Ibid.* 1911, **381**, 85; 1915, **408**, 163.

‡ It is curious that the refractive index is considerably lower than that observed for the ketone prepared from thujone. (Compare Gillam and West, *J.C.S.* 1941, p. 814.)

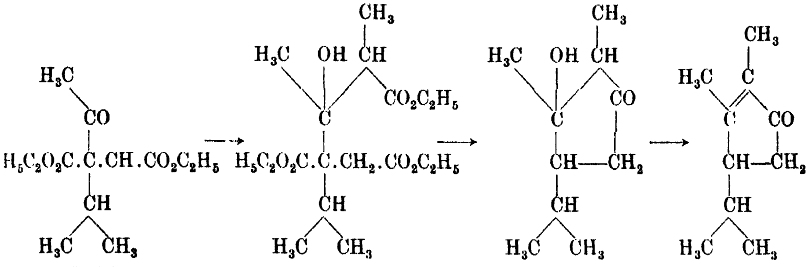


hydrazone, m.p. 137·5°). Further hydrogenation of the *cyclo*pentenol (XXXIII) gives 2:3-*dimethyl*-4-iso*propyl*cyclo*pentanol* (XXIX), b.p. 94°/12 mm., $n_D^{15°}$ 1·4649, $\alpha_D^{15°}$ −1·6° (3:5-*dinitrobenzoate*, m.p. 82–83°), which may be oxidised to 2:3-*dimethyl*-4-iso*propyl*cyclo*pentanone* (XXX), b.p. 80°/11 mm., $n_D^{17°}$ 1·4542, $\alpha_D^{18°}$ +9·9° (*semicarbazone*, m.p. 135–137°, 2:4-*dinitrophenylhydrazone*, m.p. 101·5°). These two compounds are identical with thujamenthol and thujamenthone respectively; the pronounced variation in physical constants is again presumably due to stereoisomerism, since the alcohol possesses four, and the ketone three, dissimilar asymmetric carbon atoms.

A synthesis of "Isothujon" has been described by Guha and Kuppusami.* *Ethyl β-carbethoxy-β*-iso*propyl-levulinate* (XXXIV) was condensed by the Reformatsky reaction with ethyl α-bromopropionate and the resulting product cyclised with sodium to give, in poor yield, 2:3-*dimethyl*-4-iso*propyl*-3-*hydroxy*cyclo*pentenone* (XXXV), simultaneous loss of the carbethoxy group at C_4 having occurred. Dehydration of this keto-alcohol with phosphorus pentoxide gave "Isothujon" (XXIV), b.p. 224–228° (*oxime*, m.p. 116–117°), but it is evident that the synthesis is not structurally definitive in the absence of any evidence for the direction of dehydration in the last stage.

---

* *J. Ind. Inst. Sci.* 1939, **22**, 249.


(XXXIV) (XXXV) (XXIV)

The absorption spectrum of "Isothujon" was originally thought* to be anomalous, but it was shown later† that the five-atom ring environment causes a pronounced deviation in the wave-length of maximum absorption.

A critical consideration of the evidence leaves no doubt that the constitution of thujone has been fully established, and this has more recently been confirmed by synthesis. Ruzicka and Koolhaas‡ have effected a partial synthesis from thujaketonic acid by application of the method used for the conversion of pinonic acid into pinocamphone (see p. 128). The ethyl ester (XXXVI), condensed with ethyl chloroacetate in the presence of sodium ethoxide, gave the *oxido-ester* (XXXVII) which after saponification and heating in high vacuum gave the *aldehydic acid* (XXXVIII). This was oxidised to the *dicarboxylic acid* (XXXIX), the ester of which on cyclisation with sodium gave *ethyl thujonecarboxylate* (XL). Decarboxylation was effected by boiling with aqueous barium hydroxide solution. The ketone (IX) so obtained was the *cis*-form, *d*-*iso*thujone, since it gave a *semicarbazone*, m.p. 170–172°, $[\alpha]_D$ +215°, a p-*nitrophenylhydrazone*, m.p. 148–150°, and a 2:4-*dinitrophenylhydrazone*, m.p.

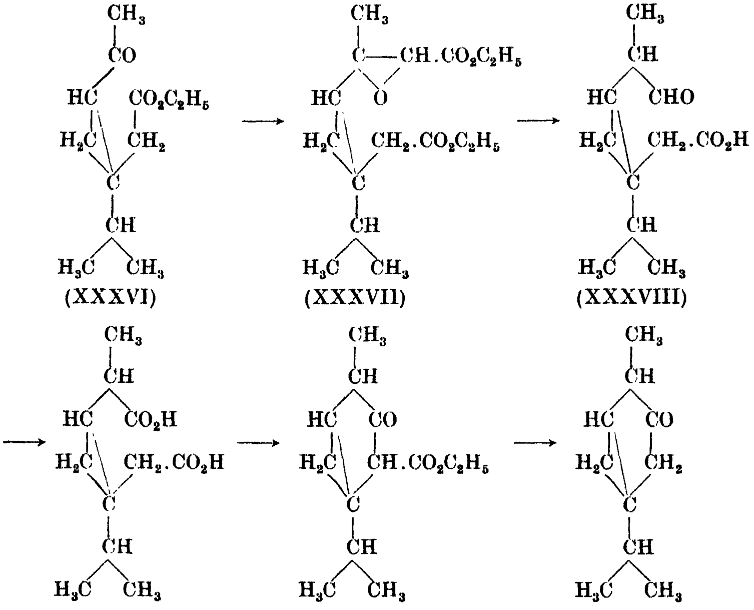
---

* Gillam and West, *J.C.S.* 1941, p. 811.

† *Idem*, *ibid.* 1942, p. 486.

‡ *Helv. Chim. Acta*, 1932, **15**, 944.

113–114°, which were identical with specimens prepared from natural *d-iso*thujone. The subsequent synthesis of α-thujaketonic acid (see p. 37) thus implies a complete synthesis of thujone.


(XXXVI) (XXXVII) (XXXVIII)

(XXXIX) (XL) (IX)

Thujone is a colourless mobile oil with a somewhat characteristic odour resembling that of menthol. When regenerated from its semicarbazone it has b.p. 201–202°/760 mm., $d_{4^\circ}^{15\cdot1^\circ}$ 0·9193, $n_D^{15^\circ}$ 1·5401, and shows a somewhat high molecular exaltation (+0·76).[*] The natural ketones, which are optically active, have been designated α- and β-thujones, the former being laevorotatory and the latter dextrorotatory, but since these are stereoisomerides it is preferable to name them l-*thujone* and d-iso*thujone* respectively.[†] Thujone shows a marked tendency to undergo inversion. Thus Paolini[‡] has shown that when *l*-thujone semicarbazone is hydrolysed with phthalic anhydride, a dextrorotatory ketone is obtained, $[\alpha]_D$ +10·23°, whilst if dilute sulphuric acid is used, as was the case in Wallach's experiments, the ketone is laevorotatory, $[\alpha]_D$ −10·23°. This is due to inversion, which can be brought about by acids and alkalis* and also by distillation in steam. Short and Read† have shown that the equilibrium position in the presence of sodium ethoxide may be represented:

---

[*] Östling, *J.C.S.* 1912, **101**, 469.

[†] Care must be taken, however, to avoid confusion with the so-called "Isothujon" of Wallach, which, as already shown, is not a bicyclic compound, and should be named systematically.

[‡] *Ann. Chim. Appl.* 1925, **15**, 414.

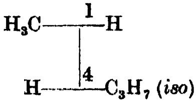
$$\text{l-}\textit{Thujone}\ (\alpha_D\ -19{\cdot}9^\circ)\ \rightleftharpoons\ \text{d-iso}\textit{Thujone}\ (\alpha_D\ +72{\cdot}5^\circ).$$
$$35\%\qquad\qquad\qquad 65\%$$

These authors have recorded the following properties for the ketones:

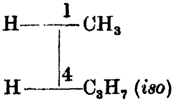
l-*Thujone:* b.p. 74·5°/9 mm., $d_{4^\circ}^{25^\circ}$ 0·9109, $n_D^{15^\circ}$ 1·4490, $\alpha_D^{18^\circ}$ −19·94° (*semicarbazone,* m.p. 186–188°, $[\alpha]_D^{15^\circ}$ +42° in methanol; 2:4-*dinitrophenylhydrazone,* m.p. 117°, $[\alpha]_D^{16^\circ}$ +44° in chloroform).

d-iso*Thujone:* b.p. 76°/10 mm., $d_{4^\circ}^{25^\circ}$ 0·9135, $n_D^{25^\circ}$ 1·4500, $\alpha_D^{18^\circ}$ +72·46° (*semicarbazone,* m.p. 172°, $[\alpha]_D^{15^\circ}$ +222° in methanol; 2:4-*dinitrophenylhydrazone,* m.p. 116°, $[\alpha]_D^{16^\circ}$ +161° in chloroform).

Although thujone contains three different asymmetric carbon atoms, it is probable that only four optically active and two racemic forms can exist, inasmuch as the presence of the *cyclo*-propane ring would involve too great a degree of strain in the other possible isomerides. In view of the fact that the two known ketones are not enantiomorphs, they must represent one optically active form of each of the two possible structures shown below, and since *l*-thujone has the lower density and refractive index it is probably the *trans*-form:



Thujone



iso*Thujone*

The calorific value of thujone is 1432 kg.-cals., identical with that of carone.‡ The absorption spectrum has been examined by Mohler and Lohr.§

---

* Wallach and Böcker, *Annalen,* 1904, **336**, 267.

† *J.C.S.* 1938, p. 2016.

‡ Roth and Östling, *Ber.* 1913, **46**, 313.

§ *Helv. Chim. Acta,* 1937, **20**, 1183.

The *enolic* form of thujone, b.p. 84–86°/12 mm., $d_{4°}^{15°}$ 0·9010, $n_D^{15°}$ 1·4540, has been prepared by Grignard and Blanchon.[*]

Thujone can be characterised most conveniently by oxidation of the appropriate fraction of the oil with potassium permanganate with formation of α-thujaketonic acid, m.p. 75–76°.

The instability of the *cyclo*propane ring structure in thujone, referred to above in considering the oxidation products, is shown generally in all its reactions. It is isomerised to carvotanacetone when heated to 200° under pressure,[†] whilst isomerisation to "Isothujon" can be brought about by many reagents in addition to sulphuric acid. Reference will be made later to some of these reactions, and attention need only be directed here to the formation of this ketone by the action of sodium[‡] and by the action of ammonium hydrogen sulphide.[§] It is also of interest to note that, according to Treibs and Schmidt,[‖] thujone distils practically without change over nickel or copper at 280°, only very little carvotanacetone being formed.

Somewhat divergent results on the hydrogenation of thujone appear in the literature, and the ketone is evidently very sensitive to slight changes in experimental conditions and the character of the catalyst. It was found by Wallach[¶] that thujone could not be reduced catalytically at the ordinary temperature, but using the Sabatier-Senderens method with a nickel catalyst at 175–180° Godchot[**] obtained a mixture of "Isothujon" and thujamenthone. Haller and Martine,[††] who used somewhat different conditions, prepared by this method thujyl alcohol. With a palladinised asbestos catalyst Zelinski and Kasansky[‡‡] succeeded in carrying the reduction further and obtained 1:2-*dimethyl*-3-iso*propyl*cyclo*pentane*. On reduction with sodium and alcohol[§§] thujone yields *thujyl alcohol*. Attempts to reduce thujone with aluminium *iso*propoxide have been unsuccessful.[‖‖]

---

[*] *Bull. Soc. chim.* 1931 [iv], **49**, 23.

[†] Semmler, *Ber.* 1892, **25**, 3344.

[‡] Schmidt, *Ber.* 1929, **62**, 106.

[§] Agostinelli, *Gazzetta,* 1913, **44**, II, 111.

[‖] *Ber.* 1927, **60**, 2338.

[¶] *Annalen,* 1911, **381**, 86.

[**] *Compt. rend.* 1914, **158**, 1807; 1921, **172**, 688; 1927, **185**, 1807.

[††] *Ibid.* 1905, **140**, 1298; compare Short and Read, *J.C.S.* 1938, p. 2016.

[‡‡] *Ber.* 1927, **60**, 1096; 1929, **62**, 2205.

[§§] Semmler, *Ber.* 1892, **25**, 3344; Short and Read, *J.C.S.* 1938, p. 2016.

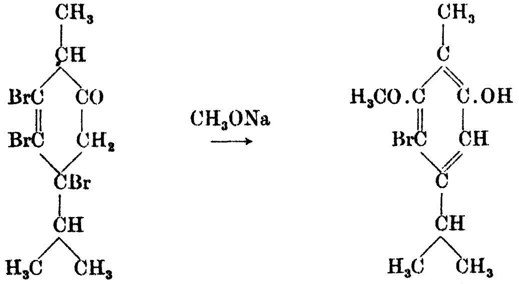
[‖‖] Short and Read, *loc. cit.*

The oxidation of thujone with potassium permanganate has been considered already (p. 36); with ferric chloride, ring fission and dehydrogenation occur with formation of carvacrol.[*]

The action of bromine on thujone was studied by Wallach,[†] who found that, in light petroleum solution, a *tribromide*, $C_{10}H_{13}OBr_3$, m.p. 121–122°, was formed. The actual constitution of this bromide has not been determined, but it is possibly represented by (XLI) since, on treatment with sodium methoxide, it yields an aromatic *bromophenol*, m.p. 156–157°, for which the constitution (XLII) has been suggested. This phenol gives an *acetyl derivative*, m.p. 64°, and a *methyl ether*, m.p. 42–43°.

According to Bruylants[‡] iodine converts thujone into *p*-cymene.

Thujone is remarkably stable to halogen acids. In ethereal solution no action occurs in the cold, but aqueous hydrochloric acid and other mineral acids isomerise it to "Isothujon", some *p*-cymene being formed simultaneously. With sodium bisulphite the ketone gives a characteristic sparingly soluble *derivative*, $C_{10}H_{16}O, NaHSO_3$, which was first prepared by Bruylants[§] and later investigated by Semmler.[‖] Since, by treatment with alkali, the ketone can be regenerated, it is very suitable for its isolation.



(XLI) (XLII)

Whereas *d-iso*thujone (β-thujone) yields a crystalline *oxime*, m.p. 54–55°, b.p. 135–136°/20 mm., $[\alpha]_D$ +105·1° (in methyl alcohol),[¶] *l*-thujone (α-thujone) gives a liquid *oxime*, which is laevorotatory, $[\alpha]_D$ −29·25° (in ether), thus providing further evidence that the two ketones are not optical enantiomorphs, but stereoisomerides of the same type as menthone and *iso*-menthone. It is not possible to regenerate thujone readily from its oxime, although hydrolysis can be effected with concentrated sulphuric acid, but the yield is poor, much of the oxime being converted into carvacrylamine. The same change occurs if the oxime is treated with zinc chloride.[*] On reduction with sodium and alcohol the crystalline oxime gives *thujylamine* (XLIII), b.p. 80·5°/14 mm., $d^{20°}$ 0·8743, $n_D^{20°}$ 1·462, $[\alpha]_D$ +101°, the same base being obtained from the liquid oxime and also by treatment of the ketone with ammonium formate.[†] The amine is not homogeneous, but a mixture of stereoisomerides, whilst that prepared by the latter reaction not improbably contains also some "*Isothujylamin*" (XLIV). Short and Read[‡] have obtained two of the stereoisomers in pure condition by fractional crystallisation of the hydrochlorides. The main product obtained by reduction of the liquid oxime is l-*thujylamine*, b.p. 81°/15 mm., $n_D^{19°}$ 1·4673, $\alpha_D^{17°}$ −24·3° (*hydrochloride*, m.p. 248–249°; p-*nitrobenzoyl* derivative, m.p. 146°; *trimethylammonium iodide*, m.p. 269°), whereas the crystalline oxime gives mainly d-iso*thujylamine*, b.p. 75°/11 mm., $n_D^{12°}$ 1·4641, $\alpha_D^{13°}$ +94·8° (*acetyl* derivative, m.p. 68–69°; *benzoyl*, m.p. 131°; p-*nitrobenzoyl*, m.p. 147°; 3:5-*dinitrobenzoyl*, m.p. 173°; *trimethylammonium iodide*, m.p. 260°). No thujyl alcohol could be obtained on treatment of these amines with nitrous acid.

---

[*] Wallach, *Annalen*, 1895, **286**, 108.

[†] *Annalen*, 1893, **275**, 179; 1895, **286**, 109.

[‡] *Ber.* 1878, **11**, 451.

[§] *Ibid.* 1878, **11**, 451.

[‖] *Ibid.* 1892, **25**, 3343.

[¶] Semmler, *Ber.* 1892, **25**, 3344; Wallach, *Annalen*, 1904, **336**, 267.

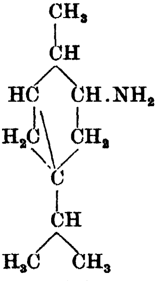
Dickison and Ingersoll[§] have investigated the products formed by the ammonium formate method, and by a lengthy fractionation of a range of salts have obtained four stereoisomers:

(A) b.p. 200°, $n_D^{25°}$ 1·4654, $\alpha_D^{25°}$ +27·8° (*benzoyl*, m.p. 73–75°);
(B) b.p. 193°, $n_D^{25°}$ 1·4564, $\alpha_D^{25°}$ +94·9° (*benzoyl*, m.p. 131°);
(C) b.p. 197°, $n_D^{27°}$ 1·4590, $\alpha_D^{27°}$ −14·1° (*benzoyl*, m.p. 94°);
(D) b.p. 202°, $n_D^{26°}$ 1·4640, $\alpha_D^{27°}$ −22·0°.

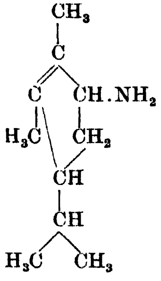
The amines (B) and (D) are probably identical with the *d-iso*thujylamine and *l*-thujylamine, respectively, of Short and Read.

---

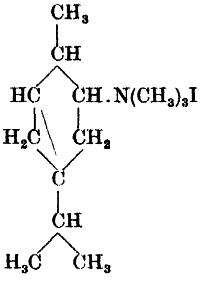
[*] Tiemann, *Ber.* 1897, **30**, 325; Wallach, *Annalen*, 1894, **279**, 383; 1895, **286**, 95.
[†] Wallach, *Annalen*, 1893, **272**, 99, 109.
[‡] *J.C.S.* 1938, p. 2016.
[§] *J. Amer. C.S.* 1939, **61**, 2477.



(XLIII)



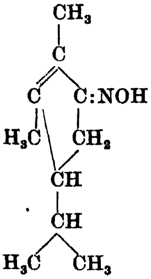
(XLIV)



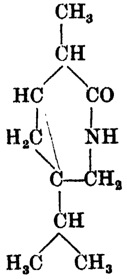
(XLV)

By the exhaustive methylation of thujylamine, Tschugaev* prepared a *trimethylthujylammonium iodide* (XLV), $[\alpha]_D$ + 42·61, which, after conversion into the hydroxide with silver oxide, gave on distillation a mixture of α- and *β-thujenes*, identical with that prepared by the distillation of methyl thujylxanthate (compare p. 11). A hydrocarbon, or mixture of hydrocarbons, is obtained also when *thujylamine hydrochloride* is distilled. This hydrocarbon, $C_{10}H_{16}$, b.p. 172–175°, $d^{20°}$ 0·840, n_D 1·4761, is probably a mixture of monocyclic hydrocarbons, but these have not been identified.

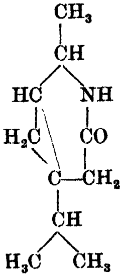
Like the parent ketone, thujoneoxime in either the crystalline or the liquid form is isomerised by concentrated sulphuric acid to "*Isothujon*" *oxime* (XLVI), m.p. 119–120°, which is optically inactive.† The crystalline oxime is converted by phosphorus pentachloride into *thujoneisoxime*, m.p. 90°.‡ The constitution of this isoxime has not been definitely established, but, if the



(XLVI)



(XLVII)



(XLVIII)

---

* *Ber.* 1901, **34**, 2276; compare Short and Read (*loc. cit.*).

† Wallach, *Annalen*, 1895, **286**, 103.

‡ *Ibid.* 1893, **277**, 159; 1895, **286**, 94; 1904, **336**, 273.

*cyclo*propane ring has not been isomerised, it is probably the dicyclic *imide* (XLVII) or (XLVIII). On reduction with sodium and alcohol it gives a *base*, $C_{10}H_{19}N$, b.p. 193°, which can be characterised by the preparation of the *phenylurethane*, m.p. 110°.

Thujone *semicarbazone* was first prepared by Baeyer,[*] who gave the melting-point as 171–172°. A more detailed investigation of this derivative by Wallach[†] has shown *d*-*iso*thujone (β-thujone) semicarbazone to be dimorphic, crystallising in hexagons, m.p. 174–175°, and rhombohedra, m.p. 170–172°, the latter modification being described as the more stable form. The value observed for the rotatory power varied somewhat, $[\alpha]_D$ +215·76° to 221·47°.[‡] *l*-Thujone (α-thujone) yields both a crystalline and an amorphous semicarbazone, the former melting at 186–188°, $[\alpha]_D$ +59·5°, whilst the latter, which was also dextrorotatory, melted about 110°.

Thujone *hydrazone* is an oil, b.p. 128–129°/18 mm., which according to Kishner[§] on reduction with sodium and alcohol gives the corresponding *hydrazine*, from which, by the action of potassium hydroxide and potassium ferricyanide, *thujane* was said to be prepared. A consideration of the constants of the hydrocarbon, b.p. 162–165°, $d_{20^\circ}^{20^\circ}$ 0·8138, $n_D^{20^\circ}$ 1·4512, $[\alpha]_D$ +3·32°, obtained by Kishner makes it very doubtful if the hydrocarbon was actually thujane. It would appear to be much more probable that it consisted essentially of 1 : 2-*dimethyl*-3-iso*propyl*cyclo*pentane* (compare p. 5). By the action of sodium ethoxide on the hydrazone, Semmler and Feldstein[||] prepared a hydrocarbon, b.p. 156–157°, $d_{21^\circ}^{22^\circ}$ 0·8158, n_D 1·4412, which undoubtedly consisted of thujane.

Advantage has been taken of the presence of a reactive methylene group adjacent to the carbonyl group to prepare from thujone a number of interesting derivatives. Haller[¶] showed that the ketone could be readily alkylated with methyl iodide (and other alkyl iodides) in the presence of sodamide to give mono-, di-, and tri-methyl derivatives. By the action of amyl formate in the presence of sodium, Wallach[*] prepared the *hydroxymethylene* derivative (XLIX), m.p. 40°, b.p. 115–118°/16 mm., whilst, by the condensation of the ketone with benzaldehyde in the presence of sodium ethoxide, Semmler[†] obtained *benzylidenethujone* (L), b.p. 176–178°/12 mm., $[\alpha]_D$ $-590{\cdot}8°$ (in alcohol), which on oxidation yields l-*homothujadicarboxylic acid* (LI), m.p. 147°.

---

[*] *Ber.* 1894, **27**, 1923.

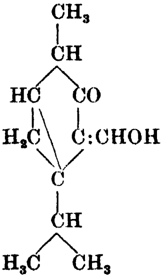
[†] *Annalen*, 1904, **336**, 253.

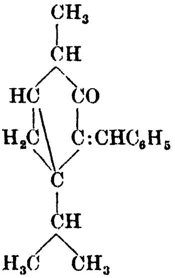
[‡] The higher value has been confirmed by Short and Read (see Table, p. 45).

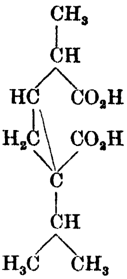
[§] *J. Russ. Phys. Chem. Soc.* 1910, **42**, 1198.

[||] *Ber.* 1914, **47**, 387.

[¶] *Compt. rend.* 1905, **140**, 1626; 1913, **157**, 965.


(XLIX)


(L)


(LI)

According to Cornubert and Borrel,[‡] if thujone is condensed with benzaldehyde in the presence of hydrogen chloride, in addition to benzylidenethujone, a "tetrahydropyrone" derivative, $C_{24}H_{26}O_2$, m.p. 115–115·5°, is also formed. The constitution of this substance would not appear to have been determined.

By the condensation of *d*-thujone with ethyl bromoacetate in the presence of zinc, Hugh and Kon[§] prepared the *hydroxy ester* (LII), from which the unsaturated *acid* (LIII) was obtained by hydrolysis and loss of water. Attempts to convert this into the isomeric acid (LIV) were not successful, ring fission occurring with formation of the cyclo*hexadiene acid* (LV). The unsaturated acid can be converted through its acid chloride into the *ketone* (LVI) which can exist also in the tautomeric form (LVII), since it can be methylated.

The action of the Grignard reagent on thujone was investigated by Thomson,[‖] who prepared a number of derivatives of thujyl alcohol.

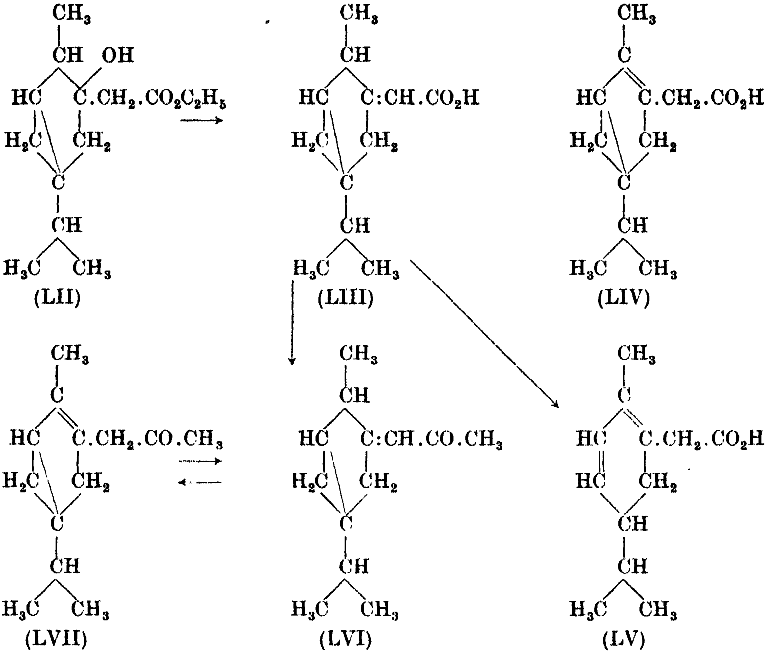
[*] *Ber.* 1895, **28**, 33.

[†] *Ibid.* 1903, **36**, 4367; compare Haller, *Compt. rend.* 1905, **140**, 1626.

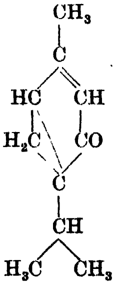
[‡] *Bull. Soc. chim.* 1929 [iv], **45**, 1148.

[§] *J.C.S.* 1927, p. 2594.

[‖] *Ibid.* 1910, **97** 1502.



UMBELLULONE



The presence of an oxygenated body boiling at about 210° in the essential oil derived from the leaves of *Umbellularia Californica* Nuttal was first observed by Heaney,* who gave to it the name oredanthol, whilst some years later Stillman† separated from this oil a fraction, b.p. 215–216°, which he designated umbellulol and which he considered to have the empirical formula, $C_8H_{12}O$. The subsequent investigations of Power and Lees[*] showed this fraction to be a mixture, the main constituent being a ketone, *umbellulone*, $C_{10}H_{14}O$. We owe the determination of the constitution of this substance to the investigations of these authors, and to Tutin and Semmler.

---

* *Amer. J. Pharm.* 1875, **47**, 105; *Pharm. J.* 1875 [iii], **5**, 791.

† *Ber.* 1880, **13**, 629; *Amer. Chem. J.* 1880, **2**, 38.

Power and Lees recognised that umbellulone was probably an unsaturated dicyclic ketone, in which the ethylenic linkage was in the $\alpha:\beta$-position to the carbonyl group, since, on treatment with semicarbazide acetate, it gave a semicarbazido-semicarbazone, and with hydroxylamine a hydroxylamino oxime, the formation of derivatives of this type being characteristic of $\alpha:\beta$-unsaturated ketones.[†] Further light on the constitution of the ketone was furnished by a study of the products formed on its oxidation with potassium permanganate, which were examined by Lees[‡] and by Tutin.[§] The main product of the oxidation is a ketonic acid, *umbellulonic acid*, $C_9H_{14}O_3$, m.p. 102°, b.p. 193–195°/50 mm., $[\alpha]_D$ +377·6° (in chloroform), which can be characterised by the preparation of the *oxime*, m.p. 169–170°. When umbellulonic acid is distilled, either at the ordinary pressure or under diminished pressure, loss of water occurs and an unsaturated *lactone*, $C_9H_{12}O_2$, b.p. 218–221°, $d^{20°}$ 1·1019, $[\alpha]_D$ −210·5°, is formed, from which umbellulonic acid can be regenerated by treatment with alkali. Oxidation of the unsaturated lactone with potassium permanganate gives a saturated dibasic acid, *umbellularic acid*, $C_8H_{12}O_4$, m.p. 120–121°, $[\alpha]_D$ −89·7° (in chloroform). This acid, which readily yields an *anhydride*, b.p. 167–169°/50 mm., is extremely stable and is not attacked by concentrated hydrochloric acid at 190°.

A consideration of these results led Tutin to suggest that umbellulone was an unsaturated dicyclic ketone containing either a dimethyl*cyclo*butane ring as in (I) or a methyl*cyclo*pentane ring (II). It was improbable that (I) could be correct, as in this case umbellularic acid should be identical with norpinic acid (V), oxidation proceeding in accordance with the scheme given below, the ketonic acid and lactone having formulae (III) and (IV) respectively.

---

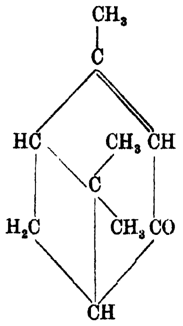
[*] *J.C.S.* 1904, **85**, 629.

[†] Harries, *Ber.* 1897, **30**, 230; Rupe and Schlochoff, *ibid.* 1903, **36**, 4377.

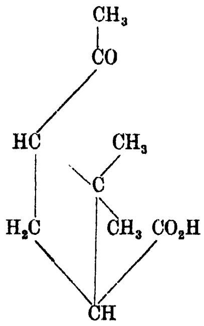
[‡] *J.C.S.* 1904, **85**, 645.

[§] *Ibid.* 1906, **89**, 1104.

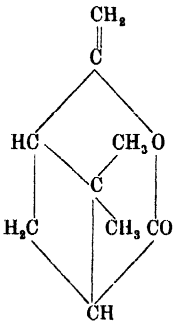
Umbellularic acid, however, differed completely in its properties from norpinic acid, and Tutin therefore concluded that umbellulone contained a *cyclo*pentane ring and assigned formulae (VI), (VII), and (VIII) to the ketonic acid, lactone and dibasic acid. The great stability of umbellularic acid led Tutin to regard the presence of a *cyclo*propane ring as unlikely.



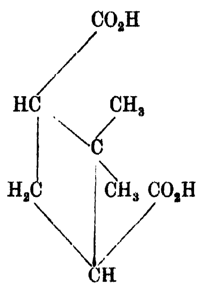
(I)



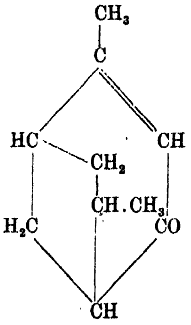
(III)



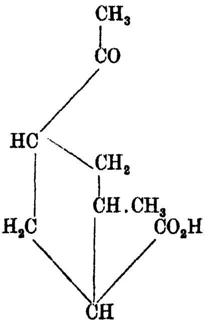
(IV)



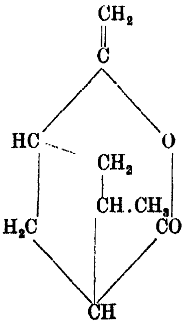
(V)



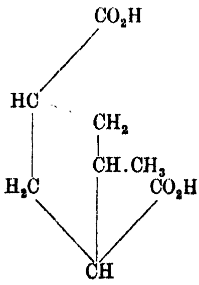
(II)



(VI)



(VII)



(VIII)

The investigation of the constitution of umbellulone was continued by Semmler.[*] It had been observed by Tutin[†] that when the ketone was reduced with sodium and alcohol a saturated secondary alcohol, *β-dihydroumbellulol*, $C_{10}H_{18}O$, was formed. Although Tutin did not succeed in purifying this alcohol, he showed that on oxidation with chromic acid it gave a ketone,

---

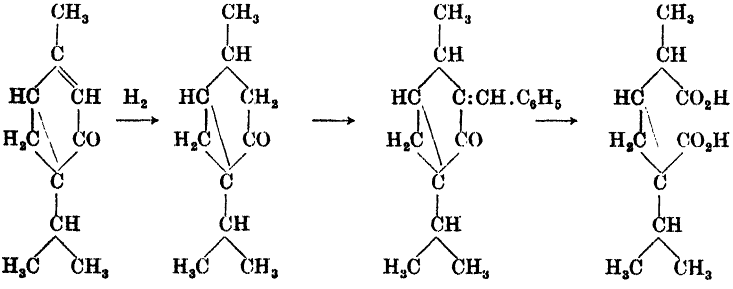
[*] *Ber.* 1907, **40**, 5019; 1908, **41**, 3988.

[†] *Loc. cit.* p. 1118.

β-dihydroumbellulone, $C_{10}H_{16}O$. This ketone was found by Semmler to have a methylene group adjacent to the carbonyl group, since it gave a *hydroxymethylene* derivative, whilst by the action of benzaldehyde a *benzylidene* derivative was prepared. When this latter derivative was oxidised with potassium permanganate, it gave a mixture of benzoic acid and d-*homothujadicarboxylic acid*, m.p. 147° (XII), the optical enantiomorph of the acid prepared from benzylidenethujone (see p. 51). The formation of this acid can only be explained if umbellulone has formula (IX), when β-dihydroumbellulone would be (X) and benzylidene-β-dihydroumbellulone (XI).

It then follows that umbellulonic acid must be the *cyclo*propane acid (XIII), the lactone (XIV) and umbellularic acid (XV). The facility with which umbellulonic acid can be converted into a lactone is now readily explained, since it may be regarded as a substituted δ-keto-acid. Attention may be directed here to the observation of Tutin* that on reduction with sodium and alcohol umbellulonic acid yields a substituted hydroxy-acid, which readily gives a *lactone*, b.p. 246–248°. This lactone must have formula (XVI), since on oxidation with potassium permanganate it gives *iso*propylsuccinic acid and acetic acid. The tendency for *cyclo*propane derivatives to undergo ring fission on treatment with reducing agents has been frequently observed.†

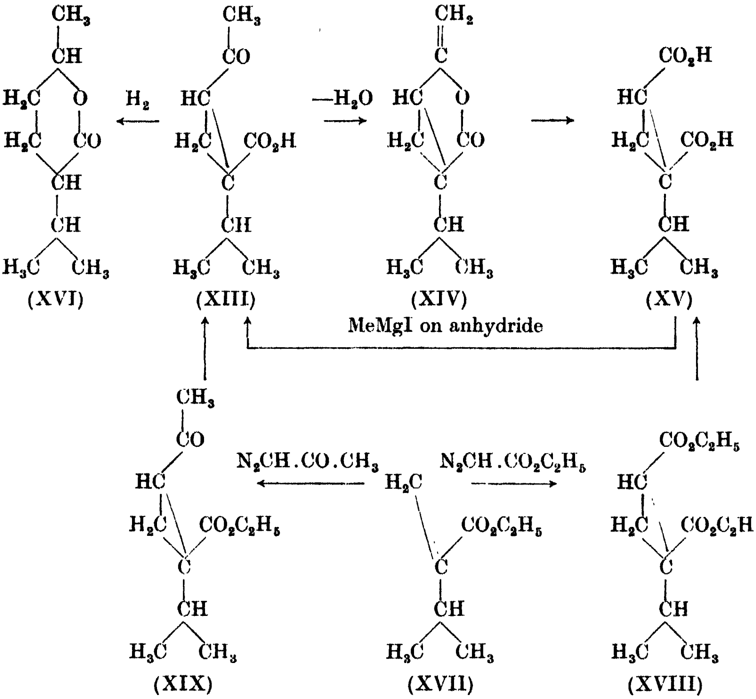
The constitutions assigned to some of these acids have now been confirmed synthetically. Umbellularic acid has been synthesised


(IX) (X) (XI) (XII)

---

* *Proc. C.S.* 1907, **23**, 28; *J.C.S.* 1908, **93**, 252.

† Compare Menon and Simonsen, *J.C.S.* 1929, p. 303, where other references to the literature are given.



by Phillips, Ramage and Simonsen* and also by Rydon.† The former authors condensed *ethyl* α-iso*propylacrylate* (XVII) with ethyl diazoacetate to give the ester (XVIII) from which on saponification was obtained dl-trans-1-iso*propyl*cyclo*propane*-1 : 2-*dicarboxylic acid*, m.p. 194–195° (p-*phenylphenacyl ester*, m.p. 175–176°), and dl-cis-1-iso*propyl*cyclo*propane*-1 : 2-*dicarboxylic acid*, m.p. 126–127° (*hydrate*, m.p. 97–98°, p-*phenylphenacyl ester*, m.p. 116–117°). The same acids were obtained by Rydon by saponification of the products of the reaction of diazomethane with diethyl *iso*propylfumarate. Resolution gave the *d*- and *l-trans* acids, m.p. 155°, $[\alpha]_{5461}$ $+232°$ and $-236°$ in acetone, and the *d*- and *l-cis* acids, m.p. 119–120°, $[\alpha]_D^{16°}$ $+86{\cdot}9°$ and $-88{\cdot}8°$ in chloroform (*hydrates*, m.p. 78–79°). The *l-cis* acid was identical with the original specimen of umbellularic acid prepared by Tutin. Similar results were obtained by

---

* *J.C.S.* 1936, p. 828.

† *Ibid.* p. 829.

Ranganathan.[*] The *dl*-acids have also been synthesised by Guha and Muthanna[†] who have, furthermore, extended the method to the synthesis of *dl-cis*-umbellulonic acid from ethyl *iso*propylacrylate (XVII) and diazoacetone, *via* the ester (XIX). The *cis*-configuration of this product was confirmed by oxidation to *dl-cis*-umbellularic acid, m.p. 124–125°. These authors[‡] have also prepared umbellulonic acid by treatment of the anhydride of *cis*-umbellularic acid with methyl magnesium iodide, and furthermore[§] have converted umbellularic acid into α-thujadicarboxylic acid.

Umbellulone is a colourless oil with a somewhat mint-like odour, which is at the same time peculiarly pungent. The ketone, regenerated from the semicarbazido-semicarbazone, has b.p. 92·5–93°/10 mm., $d^{20°}$ 0·950, $n_D^{20°}$ 1·4832, $[\alpha]_D$ −36·30°; it will be observed that it shows a very marked molecular exaltation (+1·4), due to the conjugation of the *cyclo*propane ring and the double bond. Gillam and West[‖] have found that the absorption spectrum of umbellulone is quite different from that expected of a simple αβ-unsaturated ketone, and have concluded that this is due to the cross-conjugation of the *cyclo*propane ring with the carbonyl group and the ethylenic linkage.

The ketone can be characterised by the preparation of the *semicarbazido-semicarbazone*, decomposing at 217°, or by oxidation to umbellularic acid. It can be readily isolated by taking advantage of the facility with which it combines with sodium sulphite in neutral solution, yielding a compound from which it can be regenerated by alkali.[¶]

As has been mentioned, Tutin found that, on reduction with sodium and alcohol, umbellulone gave an alcohol, *β-dihydroumbellulol*, but this was first obtained pure by Semmler,[**] who observed the constants, b.p. 88–92°/10 mm., $d^{20°}$ 0·927, $n_D^{20°}$ 1·4696, $[\alpha]_D$ −27·45°. *β-Dihydroumbellulone*, prepared from the alcohol by oxidation with chromic acid, has b.p. 84–86°/10 mm., $d^{20°}$ 0·925, $n_D^{20°}$ 1·4616, $[\alpha]_D$ −30°, *semicarbazone*, m.p. 150° (Semmler), 155–156° (Tutin). *Hydroxymethylene-β-dihydroumbellulone* is

[*] *J. Ind. C. S.* 1936, **13**, 419.

[†] *Ber.* 1938, **71** B, 2668.

[‡] *J. Ind. Inst. Sci.* 1939, **22**, 275.

[§] *Proc. Ind. Sci. Congr.* 1946, p. 67.

[‖] *J.C.S.* 1945, p. 95; compare Naves, *Helv. Chim. Acta*, 1945, **28**, 701.

[¶] Wienhaus and Todenhöfer, *Schimmel's Report*, 1929, p. 283.

[**] *Ber.* 1908, **41**, 3988.

an oil, b.p. 105–107°/10 mm., $d^{20°}$ 1·001, $n_D^{20°}$ 1·4909, whilst *benzylidene-β-dihydroumbellulone* is a solid, m.p. 81–82°, b.p. 185–188°/9 mm., $d^{20°}$ 1·030, $n_D^{20°}$ 1·574. Wienhaus and Todenhöfer* found that β-dihydroumbellulone can be conveniently prepared by the catalytic hydrogenation of umbellulone using a nickel catalyst. The ketone so obtained, b.p. 67°/4 mm., $d^{20°}$ 0·9275, $n_D^{20°}$ 1·4605, $[\alpha]_D$ −55·4°, was evidently somewhat purer than that described by Semmler and Tutin. The semicarbazone was found to melt at 158–159° and the *oxime* at 72°. On reduction with sodium and alcohol the ketone prepared in this manner gave a crystalline *β-dihydroumbellulol*, m.p. 55–56°, $[\alpha]_D$ −68·15° (in alcohol). It is possible that this is a stereoisomeride of the alcohol prepared by the direct reduction of umbellulone.

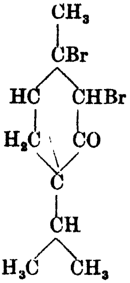
The products obtained by the oxidation of umbellulone with potassium permanganate have already been discussed and the action of other oxidising agents does not appear to have been investigated.

When umbellulone is treated in chloroform solution with bromine it yields a liquid *dibromide*,† which is somewhat unstable and gives off hydrogen bromide slowly at the ordinary temperature. If the dibromide is distilled under diminished pressure, it undergoes profound decomposition; the nature of the products which are formed in this decomposition have been investigated by Lees and Tutin and, although the latter has suggested constitutional formulae for them, these are undoubtedly incorrect and a renewed study is desirable. The distillate can be separated into three fractions: (i) a *hydrocarbon*, $C_{10}H_{14}$, which was identified as *p*-cymene, (ii) a *bromoketone*, $C_{10}H_{13}OBr$, and (iii) a *dibromodihydroumbellulone*, $C_{10}H_{14}OBr_2$. The bromoketone, b.p. 140–150°/20 mm., is apparently unsaturated, since it reacts readily with bromine in chloroform solution, although it does not react with hydrogen bromide. If the assumption be made that the removal of hydrogen bromide from the dibromide (XX) proceeds without any molecular rearrangement, the bromoketone can be most simply represented by (XXI). There can be no doubt, however, that this formula is incorrect since, when the bromoketone is reduced with zinc dust, it gives a ketone, *α-dihydroumbellulone*, b.p. 214–217°, *semicarbazone*, m.p. 171°, which is not identical with β-dihydroumbellulone (XXII), the formation of which would be anticipated if the suggested formula was correct. In the absence of any detailed description of the reactions of the bromoketone and of α-dihydroumbellulone, it is not possible to assign formulae, but it seems not improbable that each possesses a monocyclic structure.

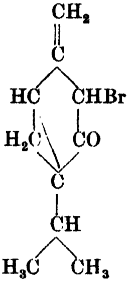
---

* *Jubiläumsbericht der Schimmel and Co.*, 1929, p. 285.

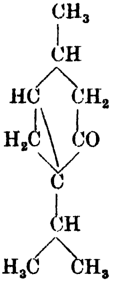
† Lees, *J.C.S.* 1904, **85**, 641; Tutin, *ibid.* 1906, **89**, 1117.



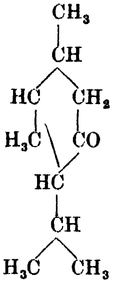
(XX)



(XXI)



(XXII)



(XXIII)

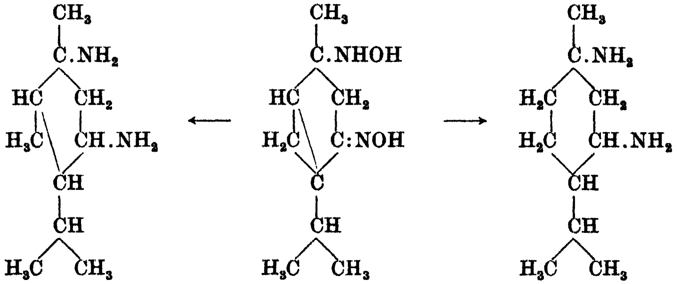
Dibromodihydroumbellulone is a crystalline substance, m.p. 119–119·5°, and it is dextrorotatory in chloroform solution, $[\alpha]_D$ +6·4°. It cannot be further brominated nor does it react with hydroxylamine; on reduction with zinc dust in acetic acid solution one bromine atom is replaced by hydrogen with formation of *bromodihydroumbellulone*, $C_{10}H_{15}OBr$, m.p. 58–59°, $[\alpha]_D$ −70·1° (in chloroform). In its general properties the monobromide resembles the dibromide and it does not react with either bromine or hydroxylamine. By further reduction with sodium in alcoholic solution an alcohol, *tetrahydroumbellulol*, $C_{10}H_{20}O$, b.p. 207–208°/760 mm., is obtained, which gives on oxidation the ketone, *tetrahydroumbellulone*, $C_{10}H_{18}O$, b.p. 197–198°. It is doubtful if this ketone is homogeneous, since it yields a *semicarbazone* separable into two fractions, m.p. 171° and 150°, although it has not been determined whether these are structural or stereoisomerides. Weinhaus and Todenhöfer* found that when β-dihydroumbellulone is reduced with sodium in toluene solution an *alcohol*, $C_{10}H_{20}O$, b.p. 80°/5 mm., $d^{20°}$ 0·902, $n_D^{20°}$ 1·4052,

---

* *Jubiläumsbericht der Schimmel and Co.*, 1929, p. 285.

α_D −38·17°, is obtained, which gives on oxidation a *ketone*, b.p. 73°/7 mm., $d^{20°}$ 0·902, $n_D^{20°}$ 1·4518, α_D −62·24°, *semicarbazone*, m.p. 177–178°. This ketone, like tetrahydroumbellulone, must be monocyclic and it is not improbable that they are identical. From analogy it seems possible that tetrahydroumbellulone and tetrahydroumbellulol are *cyclo*pentane derivatives similar to thujamenthone and thujamenthol (p. 41), in which case the ketone may be represented by formula (XXIII), tetrahydroumbellulol being the corresponding secondary alcohol. The nomenclature adopted for these substances would appear to require revision.

With semicarbazide, umbellulone yields a *semicarbazido-semicarbazone*, m.p. 217°,[*] from which the ketone can be regenerated by hydrolysis with mineral acids. The normal *semicarbazone* was prepared by Semmler[†] and melts at 240–243°. The *thiosemicarbazido-semicarbazone* has m.p. 210–211°.[‡] The *hydroxylamino-oxime* was described by Power and Lees as a resin, which according to Tutin[§] gives on reduction with sodium and alcohol a *diamine*, b.p. 136–138°/50 mm. This diamine, which was characterised by the preparation of a *dibenzyl* derivative, m.p. 194°, and a *dibenzoate*, m.p. 212–213°, has either the composition $C_{10}H_{20}N_2$ or $C_{10}H_{22}N_2$. It is probable that the reduction of the hydroxylamino-oxime (XXIV) is accompanied by ring fission, so that the diamine has either formula (XXV) or (XXVI). As the base prepared by Tutin was a mixture, it is possible that the reduction proceeds simultaneously in both directions.



(XXVI) (XXIV) (XXV)

---

[*] Power and Lees, *J.C.S.* 1904, **85**, 636.

[†] *Ber.* 1908, **41**, 3988.

[‡] Gillam and West, *J.C.S.* 1945, p. 95.

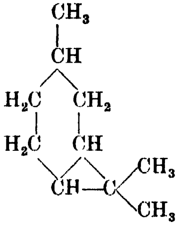
[§] *Proc. C.S.* 1907, **23**, 29.

CHAPTER II

CARANE AND ITS DERIVATIVES

A. HYDROCARBONS

CARANE[*]

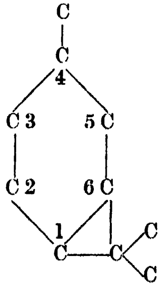


The saturated dicyclic hydrocarbon, carane, $C_{10}H_{18}$, has not been found to occur in nature. The laevorotatory hydrocarbon (I) was obtained by Kishner and Zavadovsky[†] by the distillation of *pulegonehydrazone* (II) with potassium hydroxide, whilst the dextrorotatory isomeride was prepared in a similar manner from l-*caronehydrazone* (III).[‡]

Later, Semmler and Feldstein[§] also obtained the hydrocarbon from this derivative by the action of sodium ethoxide at 140–160°. Krestinski and Solodki[‖] prepared it by the hydrogenation

---

[*] Several different methods have been used for numbering the carane system, which has unfortunately led to some confusion, particularly with regard to the nomenclature of the carenes. Δ^4-Carene, for example, has also been termed Δ^2- and even Δ^3-carene. The system adopted in the present work is based on the following skeleton formula:



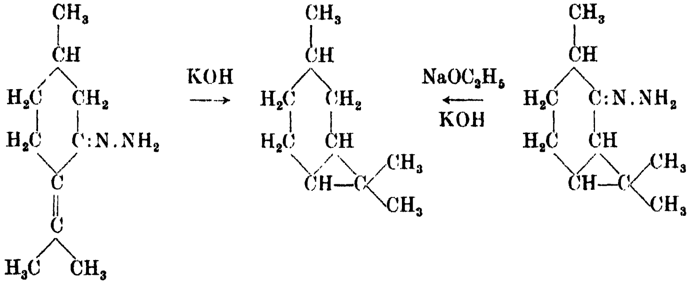
[†] *J. Russ. Phys. Chem. Soc.* 1911, **43**, 1132.

[‡] Kishner, *ibid.* p. 1554.

[§] *Ber.* 1914, **47**, 387.

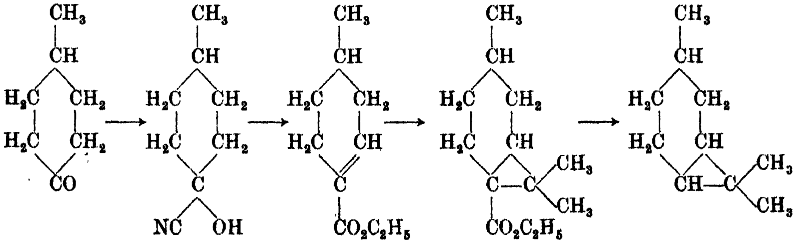
[‖] *J. pr. Chem.* 1930 [ii], **126**, 14.

of *d*-Δ^3-carene in the presence of platinum black, but from its physical constants the product would appear to have been somewhat impure.



(II) (I) (III)

dl-Carane has been synthesised by Guha and Sankaran* from 4-*methyl*cyclo*hexanone* (IV) which was converted *via* the cyanohydrin (V) into ethyl 4-*methyl*cyclo*hexenecarboxylate* (VI). Reaction with dimethyldiazomethane introduced the *cyclo*propane ring, and the resulting ester (VII) was saponified and decarboxylated to give carane (I), b.p. 162°/684 mm., $d^{26°}_{26°}$ 0·836, n_D 1·455.



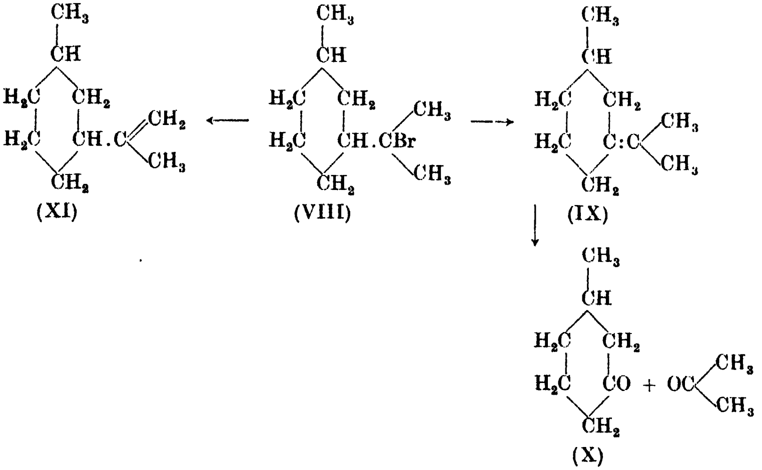
(IV) (V) (VI) (VII) (I)

Carane is a colourless mobile oil which, according to Kishner, has the following constants: b.p. 169·5°/759 mm., $d^{20°}_{0°}$ 0·8411, $n^{20°}_D$ 1·4567, $[\alpha]_D$ +57·64°, −47·06°. It is improbable that either specimen was optically pure. Semmler and Feldstein found somewhat different values, b.p. 49–50°/9 mm., 165–166°/750 mm., $d^{20°}_{20°}$ 0·8381, n_D 1·4582, $[\alpha]_D$ −34°; the latter boiling-point would appear to be somewhat low.

---

* *Ber.* 1938, 71, 2673.

Owing to the difficulties involved in its preparation, the reactions of carane have been little studied. According to Kishner and Zavadovsky, when hydrogenated by the Sabatier-Senderens process it yields solely *m*-menthane and no *p*-menthane. This result is, however, at direct variance with the observations of Zelinski and Lewina,* who claimed that when the hydrocarbon is distilled in a current of hydrogen over palladinised charcoal at 160° only *p*-menthane is formed. Whilst the difference in experimental conditions employed may account for these divergent results, it seems not improbable that in both cases the reduction product consisted of a mixture of *m*- and *p*-isomerides. Carane is readily dehydrogenated by distillation in a current of carbon dioxide over heated platinised charcoal.



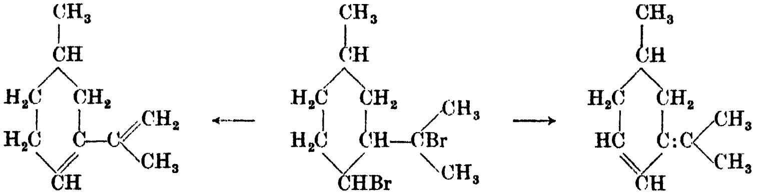
(XI) (VIII) (IX) (X)

By the action of hydrogen bromide on *d*-carane, Kishner and Zavadovsky obtained by ring fission a monohydrobromide, which they considered to be 8-*bromo*-m-*menthane* (VIII), b.p. 123–124°/29 mm., since by the action of quinoline a hydrocarbon or mixture of hydrocarbons was obtained, one of which must have been $\Delta^{3(8)}$-m-*menthene* (IX), as on oxidation with potassium permanganate it gave acetone and *methyl*cyclo*hexan*-3-*one* (X). The isomeric hydrocarbon (XI) was probably also present in the original reaction mixture. It would appear somewhat remarkable, in view of the action of hydrogen chloride on Δ^3- and Δ^4-carenes (see pp. 66, 76) that carane should only yield *m*-menthane derivatives when treated with hydrogen bromide.

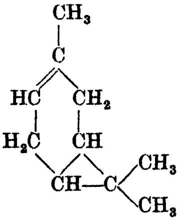
---

* *Annalen*, 1929, **476**, 60; *Chem. Zentr.* 1935, II, 3650.

Derivatives of *m*-menthane were also prepared by Kishner and Zavadovsky by the action of bromine on *d*-carane, when a *dibromide* ($[\alpha]_D$ +22·58°) was obtained, which they regarded as having the constitution (XII), since, when it was heated with quinoline, it gave m-*menthadiene*, b.p. 180–183°, $d_{4°}^{20°}$ 0·8471, $n_D^{20°}$ 1·4890. For this *m*-menthadiene, which resinifies when distilled over sodium, Kishner suggested either formula (XIII) or (XIV). Rigid proof has not been obtained of either of these structures and there does not appear to be any evidence that the dibromide was homogeneous and free from isomeric *p*-menthane derivatives.


(XIV) (XII) (XIII)

Δ^3-*CARENE*



The presence of sylvestrene in the essential oil derived from the oleo-resin of *Pinus longifolia* was reported by a number of investigators,* but Robinson† suggested that the main hydrocarbon constituent of this oil was not sylvestrene, but an isomeric terpene which gave sylvestrene dihydrochloride when treated with hydrogen chloride. The investigations of Simonsen and his collaborators[*] have shown Robinson's suggestion to be correct; the oil from *P. longifolia* does not contain *d*-sylvestrene, but a dicyclic hydrocarbon, d-Δ^3-*carene*, which, when treated with hydrogen chloride, gives a mixture of d-*sylvestrene dihydrochloride* and *dipentene dihydrochloride*. *d*-Δ^3-Carene has since been shown to occur fairly frequently in nature and has been found in Swedish oil of turpentine,[†] in various German pine-needle oils,[‡] in Finnish oil of turpentine[§] and in the oil from *P. Merkusii*,[||] whilst *l*-Δ^3-carene was separated by Panicker, Rao and Simonsen[¶] from the oil present in the rhizomes of *Kaempferia galanga* and by Krestinski, Liverovski and Malmberg[**] from a *P. sylvestris* oil.

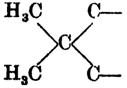
---

* Rabak, *Pharm. Rev.* 1905, **23**, 229; *Schimmel's Report,* 1906, April, p. 66; 1911, Oct. p. 93; *Bull. Imp. Inst.* 1911, **9**, 8.

† *Proc. C.S.* 1911, **27**, 247.

The constitution of Δ^3-carene has been deduced from a study of the products formed on oxidation with potassium permanganate and ozone and by its reaction with hydrogen chloride. When the hydrocarbon is oxidised with potassium permanganate in acetone solution, in addition to neutral products, to which reference will be made later, a complex mixture of acids is obtained which can be separated by fractionation of the ethyl esters into (i) *dimethylmalonic acid*, (ii) as-*dimethylsuccinic acid*, (iii) cis- and trans-*caronic acids*, (iv) a *dibasic acid*, $C_8H_{12}O_4$, m.p. 136–137°, and (v) two laevorotatory *hydroxy-dibasic acids*, $C_{10}H_{16}O_5$, m.p. 133° and 192° respectively.

Whilst the separation of dimethylmalonic acid and *as*-dimethylsuccinic acid showed the presence of the grouping



in the hydrocarbon, the isolation of the caronic acids (IV), which had been synthesised by Perkin and Thorpe,[††] proved that the terpene must contain a *cyclo*propane ring in addition to the *cyclo*hexane ring, the presence of which was shown by the formation of *sylvestrene* and *dipentene dihydrochlorides* (V) and (VI) by the action of hydrogen chloride. These results can be explained most simply by assigning to the hydrocarbon either of the three formulae (I), (II) or (III), since degradation of each of these would give caronic acid, whilst addition of hydrogen chloride to the ethylenic linkage, followed by fission of the *cyclo*propane ring, which can occur in two directions, would furnish the two hydrochlorides.

---

[*] *J.C.S.* 1920, **117**, 570; 1923, **123**, 549; 1928, p. 359; 1929, p. 305.

[†] Rao and Simonsen, *J.C.S.* 1925, **127**, 2494; compare Wienhaus and Schmidt, *Schimmel's Report*, 1928, p. 101.

[‡] Semmler and v. Schiller, *Ber.* 1927, **60**, 1591.

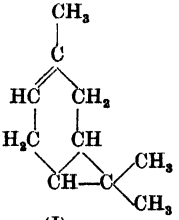
[§] Aschan, *Annalen*, 1928, **461**, 1.

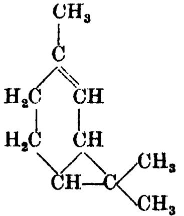
[||] Simonsen, *Ind. For. Rec.* 1923, **10**, 56.

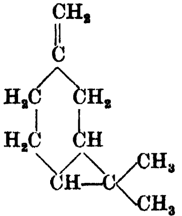
[¶] *J. Ind. Inst. Sci.* 1926, **9** A, 137.

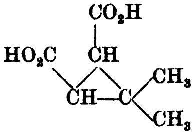
[**] *J. pr. Chem.* 1931 [ii], **129**, 97.

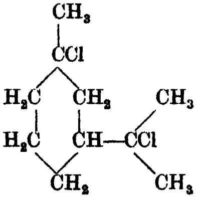
[††] *J.C.S.* 1899, **75**, 48. The resolution of *dl-trans*-caronic acid has been carried out by Owen and Simonsen, *J.C.S.* 1933, p. 1224

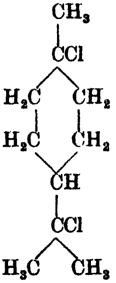

(I)


(II)


(III)


(IV)

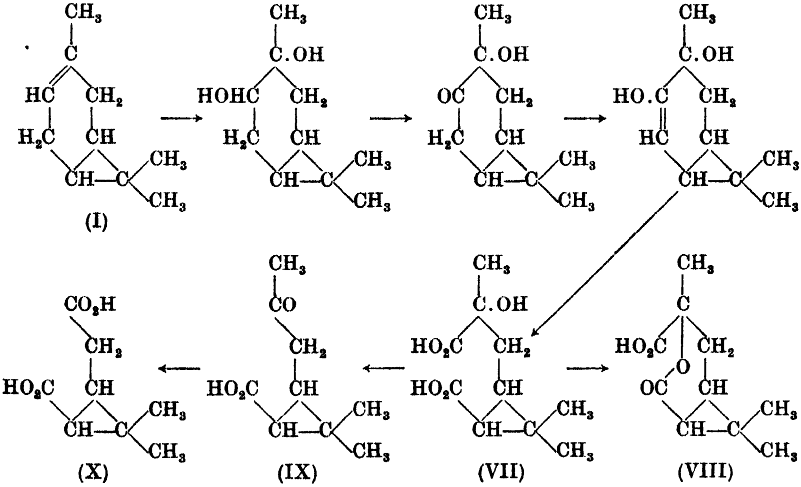

(V)


(VI)

Whilst it is clearly difficult to distinguish between the two hydrocarbons (I) and (II), the formation of the two hydroxy-acids mentioned above appears to indicate conclusively that (II) and (III)[*] cannot be correct. These two acids, α-1-α-*hydroxy-3-carboxy*-α-1 : 1-*trimethyl*cyclo*propane-2-propionic acid,* m.p. 132–133°, $[\alpha]_D$ $-8{\cdot}7°$ (in chloroform) and β-1-α-*hydroxy*-3-*carboxy*-α-1 : 1-*trimethyl*cyclo*propane-2-propionic acid*, m.p. 192°, $[\alpha]_D$ $-24{\cdot}36°$ (in chloroform), were found to be stereoisomeric α-hydroxy acids, since, although they were both quite stable to potassium permanganate in alkaline solution, they were oxidised by this reagent in acid solution to isomeric ketonic acids. Both these acids were oils, but they could be characterised readily by the preparation of the crystalline semicarbazones; that derived from the α-acid, cis-1 : 1-*dimethyl*-2-*β*-*ketopropyl*cyclo*propane*-3-*carboxylic acid*, yielding a *semicarbazone*, m.p. 179–180°, which was optically inactive, whilst from the β-acid, *l*-trans-1 : 1-*dimethyl*-2-*β*-*ketopropyl*cyclo*propane*-3-*carboxylic acid*, *semicarbazone*, m.p. 209°, $[\alpha]_D$ −70·98° (in acetic acid), was obtained. The two hydroxy acids must therefore be represented by (VII), being formed from the hydrocarbon in accordance with the following scheme, which is analogous to the oxidation of α-terpinene to αδ-dihydroxy-α-methyl-δ-*iso*propyladipic acid* (see Vol. I, p. 178).

---

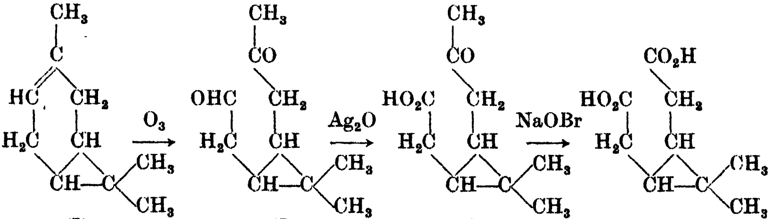
[*] According to Joffre (*Bull. Inst. Pin*, 1931, p. 79; 1932, p. 142) a hydrocarbon having this constitution occurs mixed with d-Δ^3-carene in the oil from *P. longifolia*. The quantity present is, however, very small.



The hydroxy-acids are probably *cis-trans*-isomerides, the lower melting form being the *cis*-modification, since when heated with acetyl chloride it yields a *lactone* (VIII), m.p. 174–175°, partial conversion into the *trans*-modification occurring simultaneously. It follows, then, that the two ketonic acids are the *cis*- and *trans*-forms of the acid (IX). Oxidation of the *cis*-acid with sodium hypobromite gave a dibasic acid, which is probably cis-*homocaronic acid* (X), m.p. 136–137°, identical with the dibasic acid, to which reference was made above (p. 65) as having been separated from the primary products of the permanganate oxidation. Although *cis*-homocaronic acid is not acted upon by bromine in chloroform solution, it is somewhat readily attacked by potassium permanganate in alkaline solution.[*] Homocaronic acid has been synthesised by Owen and Simonsen[†] from ethyl Δ^{β}-*iso*hexenoate and ethyl diazoacetate, and separated into the *cis*- and *trans*- forms, the former being identical with that obtained from *d*-Δ^3-carene. The acid has also been synthesised by Guha and Sankaran[‡] from ethyl glutarate and dimethyldiazomethane. Further evidence in support of the view that formula (I) correctly represents the constitution of the hydrocarbon obtained from *P. longifolia* was furnished by its oxidation with ozone.[§] With this reagent the oxidation proceeds normally, and on decomposition of the ozonide a *ketonic aldehyde*, $C_{10}H_{16}O_2$ (XI), b.p. 125–130°/12 mm., *disemicarbazone*, m.p. 198–199° (decomp.), was obtained. Oxidation of the aldehyde with either potassium permanganate or silver oxide gave the *ketonic acid*, $C_{10}H_{16}O_3$ (XII), b.p. 175–182°/12 mm., *semicarbazone*, m.p. 182–183°, which on oxidation with sodium hypobromite gave the *dibasic acid*, $C_9H_{14}O_4$ (XIII), m.p. 112–113°, whilst with potassium permanganate *cis*-caronic acid was obtained.

---

* Wallach, *Annalen*, 1907, **360**, 206; 1908, **362**, 263.



(I) (XI) (XII) (XIII)

Although direct synthetic evidence of the constitution of Δ^3-carene and of its degradation products, with the exception of the caronic and homocaronic acids, is not available, there would appear to be no doubt that it is correctly represented by formula (I).

---

[*] Compare Hariharan, Menon and Simonsen, *J.C.S.* 1928, p. 431.

[†] *J.C.S.* 1933, p. 1225.

[‡] *Ber.* 1937, **70**, 1688.

[§] Semmler and Schiller, *Ber.* 1927, **60**, 1591.

Δ^3-Carene is a colourless mobile oil with a curious sweet and penetrating odour. Simonsen observed the following constants: b.p. 168–169°/705 mm., 123–124°/200 mm., $d_{30^\circ}^{30^\circ}$ 0·8586, $n_D^{30^\circ}$ 1·468, $[\alpha]_D$ + 7·69°, whilst Dupont,[*] who obtained the hydrocarbon from the same source, gives the values, b.p. 170°/760 mm., $d_{15^\circ}^{15^\circ}$ 0·8668, $n_D^{25^\circ}$ 1·4675. The molecular refraction is normal and so in good agreement with the formula. In acetic anhydride solution the hydrocarbon gives with sulphuric acid a transient purple-green coloration.

Δ^3-Carene can be very readily characterised, since it forms a sparingly soluble *nitrosate*, m.p. 147·5° (decomp.).

The dehydrogenation of Δ^3-carene, both in liquid and vapour phase, to *p*-cymene, has been recorded by Guha, Roy and Paul,[†] whilst when refluxed over activated clay the hydrocarbon is converted into dipentene, together with a small amount of carvestrene.[‡]

The reduction of *d*-Δ^3-carene to the saturated dicyclic hydrocarbon, carane, has been found by Krestinski and Solodki[§] to proceed smoothly in the presence of platinum black (compare p. 61).

Δ^3-Carene oxidises with remarkable ease and resinifies somewhat rapidly on exposure to the air. The rate of oxidation of the hydrocarbon, both in air and in oxygen, has been studied by Rau,[‖] who found that in oxygen 18 per cent. of the gas is absorbed in 24 hours. The oxidation can be inhibited by the addition of a trace of pyrogallol, no action taking place for about 30 days, the reaction then commencing and proceeding to completion at the normal rate. The products of the autoxidation of Δ^3-carene have been investigated by Owen and Simonsen.[¶]

The oxidation of *d*-Δ^3-carene with hydrogen peroxide was investigated by Pillay and Simonsen,[**] who showed the main product of the reaction to be a glycol, d-*carene-β-glycol*, m.p. 90–91°, which was optically inactive. An isomeric glycol, d-*carene-α-glycol*, m.p. 69–70°, $[\alpha]_D$ + 16·05° (in chloroform), had been prepared previously by Simonsen by the oxidation of

---

[*] *Ann. chim.* 1924 [x], **1**, 184.

[†] *J. Ind. Inst. Sci.* 1944, **7**, 1.

[‡] Rudakoff and Artamonoff, *J. Gen. Chem. Russ.* 1945, **15**, 75.

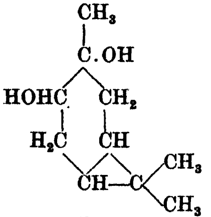
[§] *J. pr. Chem.* 1930 [ii], **126**, 14.

[‖] *Ind. For. Rec.* 1924, **9**, 203.

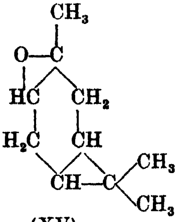
[¶] *J.C.S.* 1931, p. 3001.

[**] *Ibid.* 1928, p. 359.

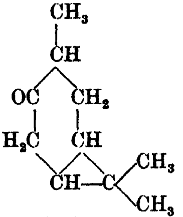
d-Δ^3-carene with potassium permanganate in alkaline solution. These two glycols are in all probability stereoisomerides having formula (XIV). They do not react with phthalic anhydride in benzene solution, but the β-glycol reacts with this reagent at 110° to give a *hydrogen phthalate*, m.p. 191–192°. When treated with dilute sulphuric acid at 100° this glycol yields a mixture of *p*-cymene and an oil, b.p. 150–153°/99 mm., $d_{30^\circ}^{30^\circ}$ 0·961, $n_D^{30^\circ}$ 1·4740, $[\alpha]_D$ $-39{\cdot}16^\circ$, which is not homogeneous but consists essentially of d-*carene oxide* (XV). This oxide reacts with phthalic anhydride at 110° to give d-*carene-β-glycol hydrogen phthalate*, m.p. 191–192°, whilst, when allowed to remain with semicarbazide acetate for some months, it gives a *semicarbazone*, $C_{11}H_{19}ON_3$, m.p. 193–193·5°, which is probably derived from the ketone (XVI). *d*-Carene oxide is remarkably stable and cannot be reconverted into the glycol by the action of sulphuric acid.



(XIV)



(XV)



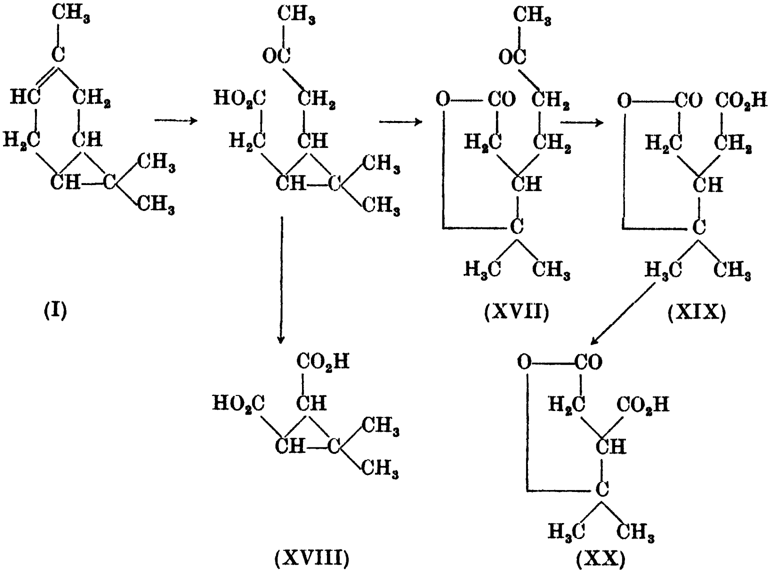
(XVI)

An isomeric oxide having somewhat different properties, b.p. 126–127°/103 mm., $d_{0^\circ}^{20^\circ}$ 0·9464, $[\alpha]_D^{20^\circ}$ $+13{\cdot}05^\circ$, has been prepared by Arbusov and Michailov* by the oxidation of *d*-Δ^3-carene with perbenzoic acid. This oxide is much less stable than that described by Pillay and Simonsen, since it yields the β-glycol when treated with dilute sulphuric acid and rearranges to an unsaturated aldehyde (*semicarbazone*, m.p. 210°) instead of the ketone (XVI). The relationship of these two oxides has not been determined. This oxide can be obtained also by the oxidation of the hydrocarbon with peracetic acid in ethereal solution.

Oxidation of *d*-Δ^3-carene with Beckmann's chromic acid mixture has been found to give a mixture of d-*homoterpenyl methyl ketone* (XVII), *l*-trans-*caronic acid* (XVIII), *terpenylic acid* (XIX) and *terebic acid* (XX), the reaction proceeding in accordance with the scheme shown below.*

---

* *J. pr. Chem.* 1930 [ii], **127**, 1; *J. Gen. Chem. Russ.* 1939, **9**, 255.



(I) (XVII) (XIX) (XVIII) (XX)

The formation of *l*-*trans*-caronic acid in this oxidation is of peculiar interest, since the ketonic acid, from which it must originate, would probably have the *cis*-configuration. Under the experimental conditions this configuration must be presumed to be unstable, passing into the *trans*-form, which is then further oxidised to the *trans*-dibasic acid.

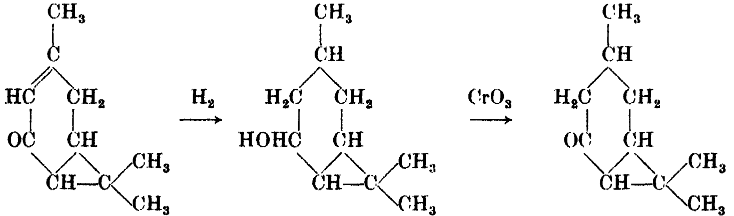
Mention has been made already of the principal products which are formed when *d*-Δ^3-carene is oxidised with potassium permanganate in acetone solution; attention must, however, be directed to an unsaturated dicyclic *ketone*, $C_{10}H_{14}O$, b.p. 110–123°/10 mm., d^{20° 1·020, $n_D^{20^\circ}$ 1·498, $[\alpha]_D$ $-5{\cdot}28^\circ$, *semicarbazone*, m.p. 159–161°, which Semmler and Schiller separated from the neutral oxidation products. This ketone is considered to be represented by formula (XXI); on reduction with sodium and alcohol it gives the saturated *alcohol*, $C_{10}H_{18}O$ (XXII), b.p. 103–108°/11 mm., d^{20° 0·9262, $n_D^{20^\circ}$ 1·476, from which, by oxidation with chromic acid, the saturated *ketone*, $C_{10}H_{16}O$ (XXIII), b.p.

---

* Gibson and Simonsen, *J.C.S.* 1929, p. 305.

88–100°/11 mm., d^{20° 0·9262, $n_D^{20^\circ}$ 1·476, *semicarbazone*, m.p. 223–224°, was prepared. No direct proof of the constitution of these substances is available and the formation of an unsaturated ketone by oxidation with potassium permanganate is somewhat unusual, although there are several examples of its occurrence during oxidation under other conditions.

With bromine in chloroform solution d-Δ^3-carene reacts readily, one molecule of bromine being absorbed, but the dibromide is unstable and evolves hydrogen bromide. According to Aschan[*] the hydrocarbon gives with hydrogen chloride a monohydrochloride, b.p. 75–80°/10 mm., identical with that obtained from d-Δ^4-carene (p. 76); the yield of this substance is very poor, the main product, as mentioned above, being a mixture of the dihydrochlorides of dipentene and sylvestrene. d-Δ^3-Carene is not attacked by warm dilute sulphuric acid (5 per cent.) but, if heated with this reagent in acetic acid solution at 60°, a *diterpene*, b.p. 175°/10 mm., $d_{20^\circ}^{20^\circ}$ 0·9309, $n_D^{20^\circ}$ 1·5168, $[\alpha]_{5461}$ + 5·69°, is obtained.



(XXI) (XXII) (XXIII)

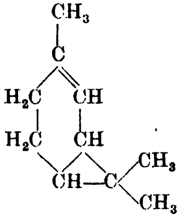
d-Δ^3-*Carene nitrosochloride* has been described by Lagache;[†] it is extremely unstable and decomposes at 101–102°. It has been characterised by the preparation of the *nitrolmethylamine*, m.p. 180°, and *nitrolaniline*, m.p. 143–144°. On digestion with sodium carbonate in alcoholic solution, it is converted into nitrosocarene, m.p. 89–90°. *Carene nitrosate*, decomposing at 147·5°, was prepared by Simonsen and, owing to its sparing solubility in organic media, it can be readily separated even when the hydrocarbon is only present in small quantity. It is extremely stable and has up to the present not been converted into nitrosocarene.

---

[*] *Annalen*, 1928, **461**, 1; compare Krestinski and Malevskaja, *J. Appl. Chem. Russ.* 1939, **12**, 878.

[†] *Bull. Inst. Pin*, 1927, p. 233.

Δ^4-*CARENE*



The hydrocarbon, *d*-Δ^4-carene, $C_{10}H_{16}$, was separated from the essential oil derived from the grass, *Andropogon Jwarancusă* Jones, by Simonsen,[*] who shortly afterwards showed it to be the main hydrocarbon constituent of an oil derived from an unidentified *Andropogon* grass occurring in the Etawah District, United Provinces, India.[†] Simonsen suggested that the terpene was probably somewhat widely distributed in nature and this has since been confirmed by its isolation from German pine-needle oil (from *Pinus sylvestris* L.) by Semmler and Schiller,[‡] from Finnish oil of turpentine,[§] from Swedish oil of turpentine[||] and from the oil of *Dacrydium Franklini* Hook. f.[¶] *l*-Δ^4-Carene has not been described.

The constitution of Δ^4-carene has been established by the investigations of Simonsen and his collaborators. When the hydrocarbon is oxidised in acetone solution with potassium permanganate it gives in excellent yield a liquid ketonic acid, $C_{10}H_{16}O_3$. This acid, which was characterised by the preparation of the *semicarbazone*, m.p. 182–183°, the *oxime*, m.p. 124–125°, $[\alpha]_D^{30°}$ $+44{\cdot}9°$ (in methyl alcohol) and the *ethyl ester*, b.p. 133–135°/11 mm., *semicarbazone*, m.p. 119–120°, is undoubtedly d-1:1-*dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid* (II), since, when oxidised with sodium hypobromite, it yields a dibasic acid, d-3-*carboxy*-1:1-*dimethyl*cyclo*propane*-2-*propionic acid* (III), m.p. 103–105°, $[\alpha]_D$ $+33{\cdot}5°$ (in chloroform). The constitution of this latter acid was proved by its conversion on treatment with hydrogen bromide into *homoterpenylic acid* (IV), which has been prepared synthetically.* If *d*-Δ^4-carene be represented by (I), the reactions involved are shown in the scheme:

---

[*] *J.C.S.* 1921, **119**, 1644; 1922, **121**, 2292.

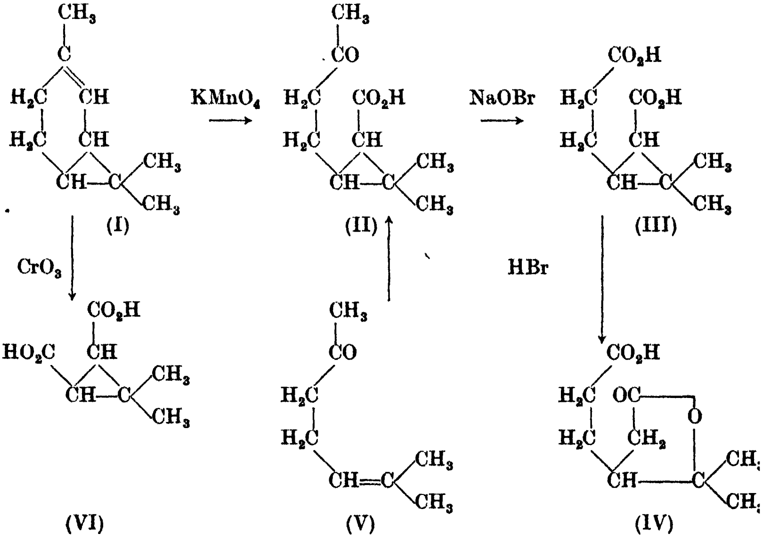
[†] *Ind. For. Rec.* 1924, **10**, 160.

[‡] *Ber.* 1927, **60**, 1591; *Schimmel's Report*, 1928, p. 97.

[§] Aschan, *Annalen*, 1928, **461**, 1. Aschan originally used the name *pinonene* for Δ^4-carene.

[||] Wienhaus and Schmidt, *Schimmel's Report*, 1928, p. 99.

[¶] Penfold and Simonsen, *J. Proc. Roy. Soc. New South Wales*, 1929, **63**, 95.



Confirmation of the structure of the acids (II) and (III) has been provided by Owen and Simonsen.† By the condensation of methylheptenone (V) with ethyl diazoacetate, and saponification of the product, the *dl-cis-* and *dl-trans*-forms of the ketoacid (II) were obtained, which with sodium hypobromite were converted into the corresponding *dl*-isomers of the dibasic acid (III). Resolution of the latter products was successfully accomplished, and the *d-cis*-acid, m.p. 104–105°, was found to be identical with that obtained from the oxidation products of *d*-Δ^4-carene.

A further direct proof of the presence of the *cyclo*propane ring in Δ^4-carene was furnished by its oxidation to l-trans-*caronic acid* (VI) by Beckmann's chromic acid mixture.‡ There can therefore be no doubt that the hydrocarbon has been correctly formulated and this is supported by its reaction with hydrogen chloride (see p. 77).

---

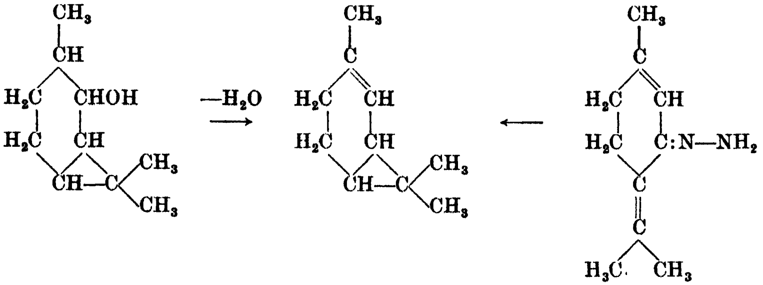
* Simonsen, *J.C.S.* 1907, **91**, 184.

† *J.C.S.* 1932, p. 1424; 1933, p. 1223.

‡ Gibson and Simonsen, *J.C.S.* 1929, p. 909.

Menon and Simonsen[*] have described the synthesis of a hydrocarbon which is probably identical with Δ^4-carene but, owing to the limited material available, confirmation by the preparation of crystalline derivatives was not obtained. When the *methyl xanthate* of l-*carol* (VII) (see p. 82) is distilled at the ordinary pressure a hydrocarbon is obtained which, as will be seen from the table, has constants agreeing very closely with those of the natural terpene.

	d-Δ^4-*Carene*	*Synthetic hydrocarbon*
B.p.	165·5–167°/707 mm.	165–170°/685 mm.
$d_{30}^{30°}$	0·8552	0·8551
$n_D^{30°}$	1·474	1·473
$[\alpha]_D^{20°}$	+62·2°	−5·96° (in acetic acid)


(VII) (I) (VIII)

dl-Δ^4-Carene has been obtained by Naves and Papazian[†] by the Kishner reaction on *piperitenone hydrazone* (VIII).

d-Δ^4-Carene is a colourless mobile oil with a pleasant odour reminiscent of *p*-cymene. The molecular refraction (44·60), in contrast to that of Δ^3-carene, shows a marked exaltation (+0·5) owing to the conjugation of the ethylenic linkage with the *cyclo*propane ring. It is, however, considerably lower than that shown by sabinene (+0·78). According to Semmler and Schiller, when the terpene is heated to 280° under pressure, it is isomerised to sylvestrene and α-terpinene.

Δ^4-Carene is said[‡] to give with maleic anhydride a liquid adduct, of which the corresponding dibasic acid has m.p. 184°, but in view of the doubtful purity of the hydrocarbon used, a further investigation of this reaction is desirable.*

---

[*] *J. Ind. Inst. Sci.* 1927, **10A**, 4; compare Ruzicka, *Helv. Chim. Acta*, 1932, **15**, 957.

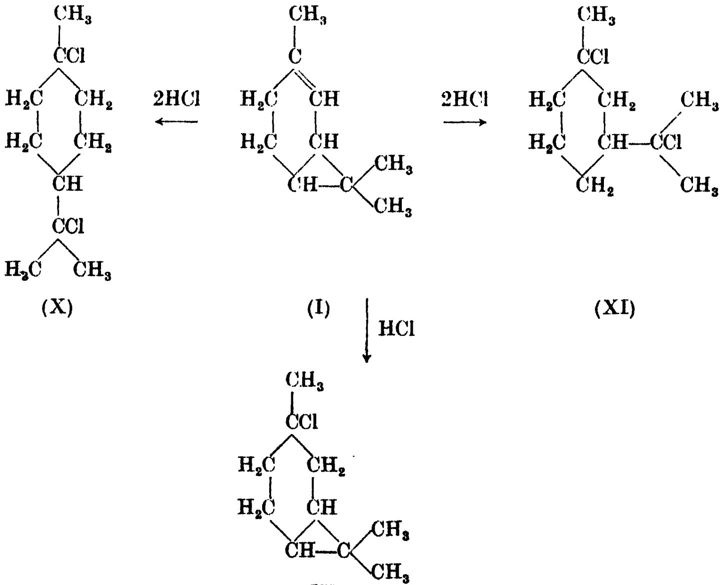
[†] *Helv. Chim. Acta*, 1942, **25**, 984.

[‡] Diels, Koch and Frost, *Ber.* 1938, **71**, 1163; Hultzsch, *ibid.* 1939, **72**, 1173.

Since Δ^4-carene does not yield any well-authenticated crystalline derivatives, it is somewhat difficult to identify. When available in sufficient quantity this is generally best effected by oxidation with potassium permanganate to the ketonic acid, $C_{10}H_{16}O_3$, or with Beckmann's chromic acid mixture to *l-trans*-caronic acid. In acetic anhydride solution it gives with sulphuric acid a transient purple colour.

No experiments have been made on the reduction of Δ^4-carene. It is very much more slowly oxidised by oxygen or air than Δ^3-carene.†

With bromine in chloroform solution it gives a liquid bromide, whilst with hydrogen chloride in ethereal solution it gives a *monohydrochloride* (IX) which according to Aschan boils at 75–80°/10 mm. In acetic acid solution, however, the hydrocarbon shows the characteristic property of carene derivatives



(X) (I) (XI)

(IX)

---

* Compare Goodway and West, *J.C.S.* 1940, p. 702.

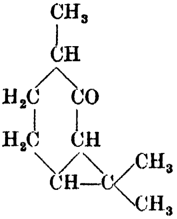
† Rau, *Ind. For. Rec.* 1924, 11, 205.

and yields a mixture of *dipentene* and *sylvestrene dihydrochlorides* (X) and (XI), the *cyclo*propane ring undergoing fission.

The question of the mechanism of the formation of Δ^4-carene in nature has been discussed elsewhere (Vol. I, p. xiv).

B. KETONES

CARONE



Reference has been made already (Vol. I, p. 215) to Baeyer's important observation* that, when dihydrocarvone hydrobromide is treated with an alcoholic solution of potassium hydroxide at 0°, elimination of hydrogen bromide occurs with the formation of a saturated dicyclic ketone, *carone*. Although the occurrence of this ketone in nature has not so far been observed, in view of the somewhat wide distribution of the related hydrocarbons, Δ^3- and Δ^4-carenes, it seems not unlikely that it may be found in essential oils.

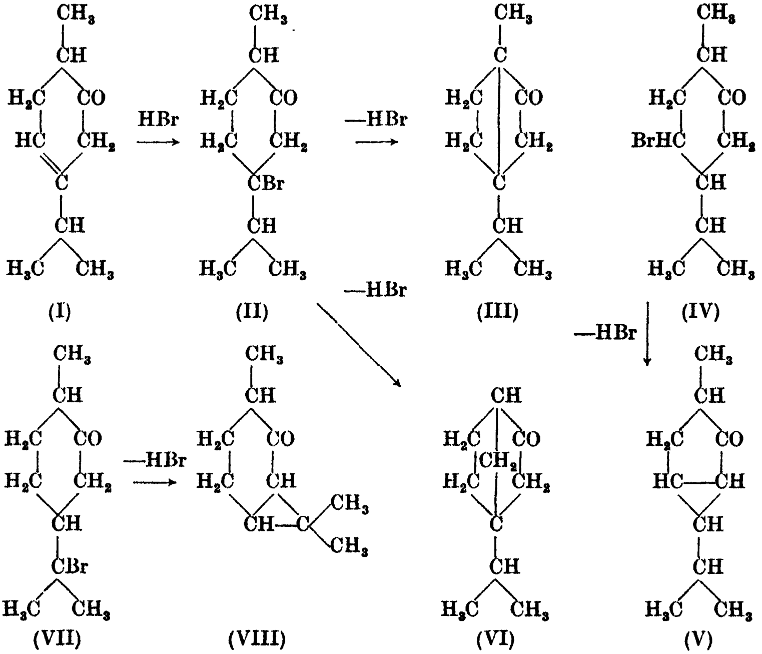
At the time of Baeyer's experiments the constitution of carvone was not definitely known (compare Vol. I, p. 394) and dihydrocarvone was given formula (I) and the hydrobromide (II). Baeyer suggested, therefore, that the new ketone might contain either a *cyclo*pentane ring as in (III) or, if the hydrobromide had the alternative formula (IV), a *cyclo*propane ring (V). In the following year† other possible formulae were discussed and, subject to (II) correctly representing dihydrocarvone, Baeyer gave preference to (VI), which was closely allied to the Bredt formula for camphor.

The recognition of the correct formula for carvone and the confirmation by Tiemann and Semmler of the presence of an

---

* *Ber.* 1894, **27**, 1919.

† *Ibid.* 1895, **28**, 1598.



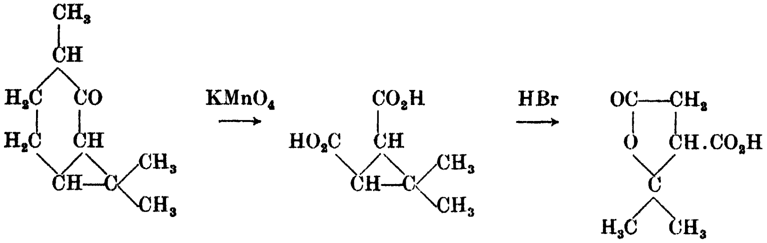
*iso*propenyl group in dihydrocarvone (Vol. I, p. 351) led Wagner[*] to formulate carone as (VIII), since it was formed by the removal of hydrogen bromide from dihydrocarvone hydrobromide (VII). Baeyer and Ipatiev[†] showed this theoretical conclusion to be correct, since they found that when the ketone was oxidised with a hot solution of potassium permanganate it gave a saturated dibasic acid, *caronic acid*, $C_7H_{10}O_4$, the *cis*-modification of which melted at 174–175°, *anhydride*, m.p. 54–56°, and the *trans*-modification at 212°. This acid was isomerised by hydrogen bromide at 100° to *terebic acid* (X) and Baeyer and Ipatiev formulated caronic acid as the *cyclo*propane acid (IX), which was confirmed by the elegant synthesis carried out shortly afterwards by Perkin and Thorpe.[‡] There can therefore be no doubt that Wagner's formula for carone is correct.

---

[*] *Ber.* 1894, **27**, 1652, 2270; *Abhandlung, Warsaw*, 1894, p. 39; *J. Russ. Phys. Chem. Soc.* 1896, **28**, 95; 1898, **30**, 259.

[†] *Ber.* 1896, **29**, 2797; compare Kondakov and Gorbunov, *J. pr. Chem.* 1897 [ii], **56**, 257.

[‡] *J.C.S.* 1899, **75**, 48.



(VIII) (IX) (X)

Carone is a colourless mobile oil with a pleasant camphoraceous odour. Both the dextro- and laevorotatory forms of the ketone have been prepared from the corresponding dihydrocarvone hydrobromides and they have the same sign as the parent unsaturated ketone. When distilled at the ordinary pressure the ketone boils at about 210° with partial decomposition and isomerisation to *carvenone*;[*] it can, however, be distilled under diminished pressure. The following constants have been recorded: b.p. 99–100°/15 mm., $d_{4^\circ}^{20^\circ}$ 0·9567, $n_D^{18\cdot8^\circ}$ 1·4787, $[\alpha]_D$ $+173\cdot8^\circ$ and $-169\cdot5^\circ$. For a specimen of the ketone, from which an unsaturated impurity had been removed by treatment with perbenzoic acid, Richter, Wolff and Presting[†] found the following values: b.p. 98°/13 mm., $d_{4^\circ}^{17^\circ}$ 0·955, $n_D^{16^\circ}$ 1·478, $[\alpha]_D$ $+134^\circ$.

The absorption spectrum of carone indicates some degree of hyperconjugation between the *cyclo*propane ring and the carbonyl group.[‡]

Carone can be identified by the preparation of the *semicarbazone*, *d*- and *l*-, m.p. 167–169°, *dl*, m.p. 178°, or by oxidation to caronic acid.

Although the *cyclo*propane ring in carone is sufficiently stable in the presence of alkali to enable caronic acid to be separated after oxidation, yet in the majority of reactions this undergoes fission with formation of either *p*- or *m*-menthane derivatives, the ketone behaving as if it contained an ethylenic linkage.

Reduction of carone to the corresponding secondary alcohol, *carol*, cannot be effected, although this alcohol has been prepared by an indirect method (p. 81). Catalytic hydrogenation of *d*-carone in the presence of colloidal palladium was found by

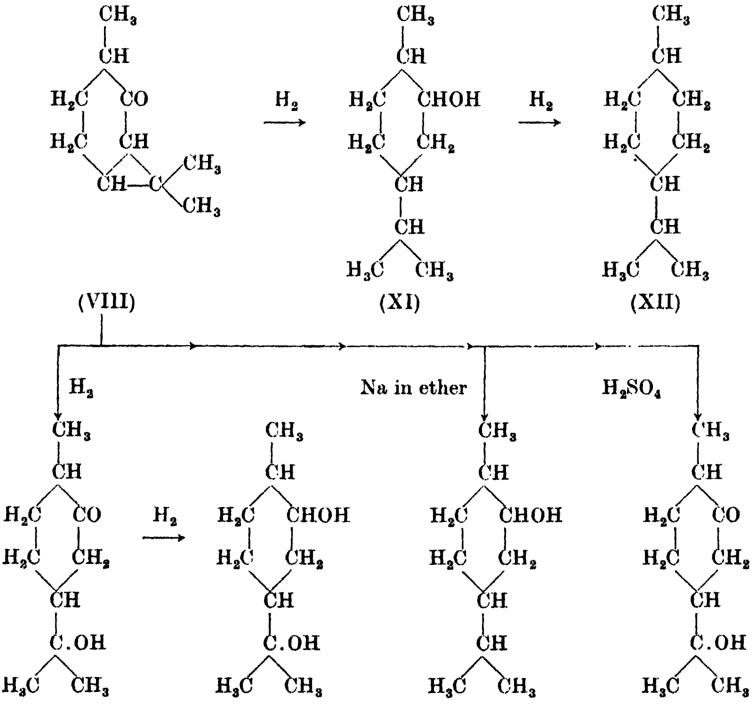
---

[*] Baeyer, *Ber.* 1894, **27**, 1920.

[†] *Ber.* 1931, **64**, 877.

[‡] Klotz, *J. Amer. C.S.* 1944, **66**, 90; Gillam and West, *J.C.S.* 1945, p. 95.

Iyer and Simonsen[*] to give a mixture of p-*menthan-2-ol* (XI), p-*menthane* (XII) and l-p-*menthane-2:8-diol* (XIV). Whilst the first two substances owe their formation to fission of the *cyclo*propane ring followed by the reduction of the carbonyl group,



(VIII) (XI) (XII)

(XIII) (XIV) (XV) (XVI)

the simultaneous formation of the diol is not so readily accounted for. It is probably due to a preliminary hydration of the dicyclic ketone by the dilute mineral acid present in the reaction mixture, the resulting 8-*hydroxycarvomenthone* (XIII) then undergoing reduction.[†] It is interesting to note that no derivatives of *m*-cymene were formed. By the reduction of carone with sodium in moist ethereal solution Baeyer[‡] obtained *carvomenthol* (XV), the *hydroxymethylene* derivative of the corresponding ketone being formed when carone was treated with ethyl formate in the presence of sodium.

---

[*] *J.C.S.* 1926, p. 2049.

[†] Compare Richter, Wolff and Presting, *Ber.* 1931, **64**, 877.

[‡] *Ber.* 1895, **28**, 1601.

Carone only reacts very slowly with bromine and does not yield any crystalline derivatives.[*] With hydrogen bromide, fission of the *cyclo*propane ring occurs with formation of a liquid hydrobromide, which was recognised by Baeyer as *dihydrocarvone hydrobromide* by the preparation of the oxime, m.p. 118–120°. According to Kondakov and Gorbunov[†] isomerisation to carvenone occurs simultaneously, but the evidence for this is not convincing and requires confirmation. A similar fission of the *cyclo*propane ring was shown by Baeyer[‡] to occur if the ketone was allowed to remain for some days with an alcoholic solution of sulphuric acid, 8-*hydroxycarvomenthone* (XVI), *semicarbazone*, m.p. 149°, being formed. By concentrated sulphuric acid carone is isomerised to carvenone.[§]

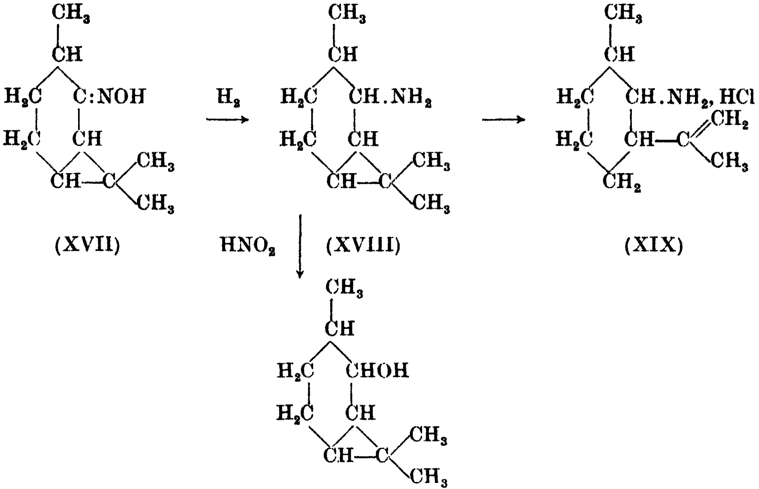
d- and l-*Caroneoximes* (XVII), which were prepared by Baeyer,[||] are oils, the following constants being given by Kondakov and Schindelmeiser[¶] for that prepared from *d*-carone: b.p. 130–132°/12 mm., $d^{20°}$ 1·018, $n_D^{20°}$ 1·4795, $[\alpha]_D$ $-255{\cdot}6°$. It will be observed that a reversal of sign of rotation occurs. The dl-*oxime* is a solid, m.p. 77–79°.

Results of great interest have been obtained from a study of the base d-*carylamine* (XVIII), which was prepared by Baeyer[**] by the reduction of *d*-caroneoxime with sodium and alcohol. The base is an oil, b.p. 88–89°/15 mm., $[\alpha]_D$ $+72{\cdot}3°$ (in alcoholic solution),[††] and gives a crystalline benzoyl derivative, m.p. 123°. When an alcoholic solution of carylamine hydrochloride is evaporated, it is isomerised yielding *vestrylamine hydrochloride* (XIX), the conversion of which into carvestrene has been discussed already (Vol. I, p. 215).

By treatment of *d*-carylamine sulphate with nitrous acid Menon and Simonsen[‡‡] prepared l-*carol* (XX), b.p. 141–142°/100 mm., $d_{30°}^{30°}$ 0·9181, $n_D^{30°}$ 1·472, $[\alpha]_D$ $-42{\cdot}92°$. *l*-Carol on oxidation

---

[*] Baeyer, *Ber.* 1894, **27**, 1920.
[†] *J. pr. Chem.* 1897 [ii], **56**, 255.
[‡] *Ber.* 1896, **29**, 6.
[§] Rimini, *Gazzetta*, 1909, **39** [ii], 199.
[||] *Ber.* 1894, **27**, 3485; 1895, **28**, 640.
[¶] *J. pr. Chem.* 1903 [ii], **68**, 112.
[**] *Ber.* 1894, **27**, 3486.
[††] Menon and Simonsen, *J. Ind. Inst. Sci.* 1927, **10**A, 3.
[‡‡] *J. Ind. Inst. Sci.* 1927, **10**A, 3.



(XVII) (XVIII) (XIX) (XX)

with chromic acid is reconverted into the parent ketone. The synthesis of Δ^4-carene from the alcohol is referred to on p. 75.

Mention may be conveniently made here of a hydroxy derivative of carone which was obtained by Baeyer[*] by the action of an alcoholic solution of potassium hydroxide on 1-*hydroxy*-8-*bromocarvomenthone* (XXI) (Vol. I, p. 356). The dicyclic *hydroxyketone* (XXII), b.p. 134–135°/19 mm., $[\alpha]_D$ +32·66°, can be characterised by the preparation of the *oxime*, m.p. 138°, *semicarbazone*, m.p. 197° and the *phenylurethane*, m.p. 190°. On treatment with hydrogen bromide, fission of the *cyclo*propane ring occurs together with replacement of the hydroxy group by bromine with the formation of 1:8-*dibromocarvomenthone* (XXIII), whilst with sulphuric acid it is hydrated to *ketoterpin* (XXIV), m.p. 78–80°. The constitution of this ketone was proved by its reduction to p-*menthane*-1:2:8-*triol* (XXV), which on oxidation gave *homoterpenyl methyl ketone* (XXVI).

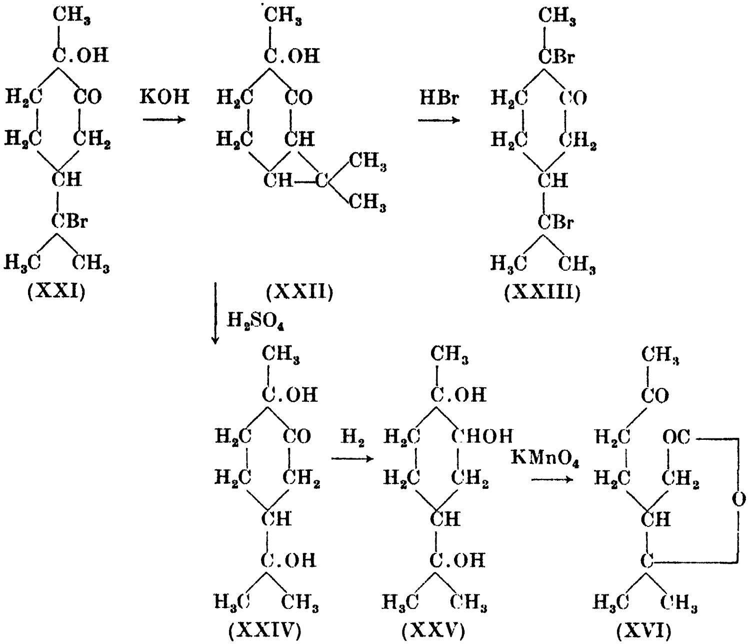
Carone was found by Baeyer to react very readily with semicarbazide[†] to yield a highly characteristic *semicarbazone*, m.p. 167–169°, *dl*-form, m.p. 178°. The *thiosemicarbazone* melts at 131–132°.[‡]

---

[*] *Ber.* 1898, **31**, 3211.

[†] *Ibid.* 1895, **28**, 641.

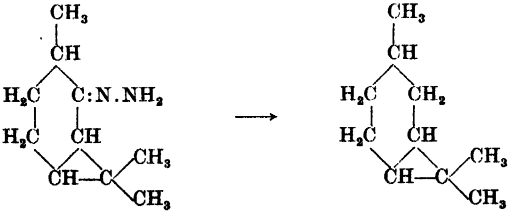
[‡] Gillam and West, *J.C.S.* 1945, p. 98.



(XXI) (XXII) (XXIII)

(XXIV) (XXV) (XVI)

d-*Carone hydrazone* (XXVII) is an oil, b.p. 131°/20 mm., $d^{20°}$ 0·9683, $n_D^{20°}$ 1·5082, which, according to Kishner,* when boiled with dilute sulphuric acid yields carvenone, and when distilled with potassium hydroxide gives the saturated dicyclic hydrocarbon, l-*carane* (XXVIII), b.p. 169°/761 mm., $d^{20°}$ 0·8411, $n_D^{20°}$ 1·4569, α_D $-47·06°$. The conversion of carone hydrazone into *l*-carane also occurs when it is heated with sodium ethoxide under pressure.†



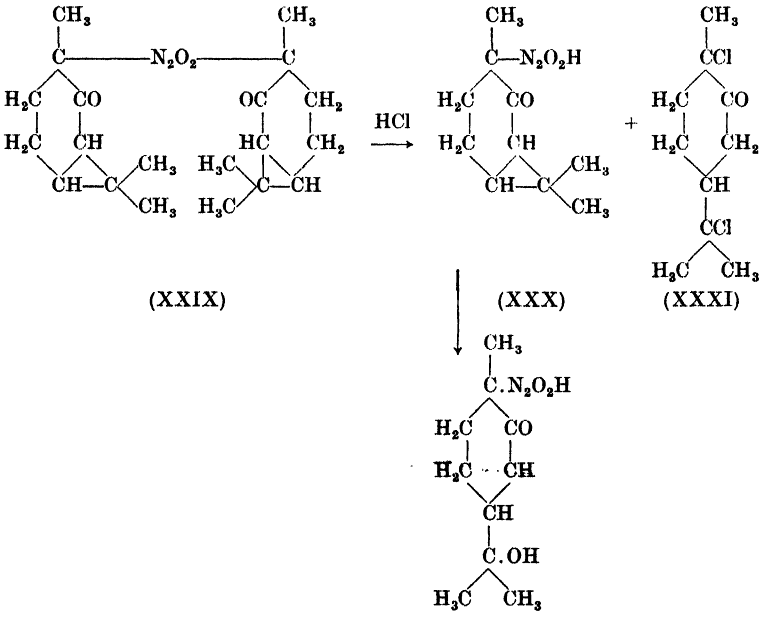
(XXVII) (XXVIII)

---

* *J. Russ. Phys. Chem. Soc.* 1911, **43**, 1554.

† Semmler and Feldstein, *Ber.* 1914, **47**, 386.

Of peculiar interest is the derivative of carone, ***bis-nitrosocarone*** (XXIX), which Baeyer[*] prepared by the action of acetyl chloride on a mixture of the ketone and *iso*amyl nitrite, since this was the first derivative of this type to be investigated. Bis-nitrosocarone is a crystalline solid, the *d*- and *l*-forms decomposing at 116–118° and the *dl*- at 148°. When it is treated with an alcoholic solution of hydrogen chloride, it gives a mixture of the *nitrosylic acid* (XXX), m.p. 80–90°, and 1:8-*dichlorocarvomenthone* (XXXI), m.p. 42°. As might be anticipated the *cyclo*propane ring in the nitrosylic acid is unstable, and when the acid is distilled in steam it is hydrated, yielding *hydroxycarvomenthone nitrosylic acid* (XXXII), m.p. 184°.[†]


(XXIX) (XXX) (XXXI) (XXXII)

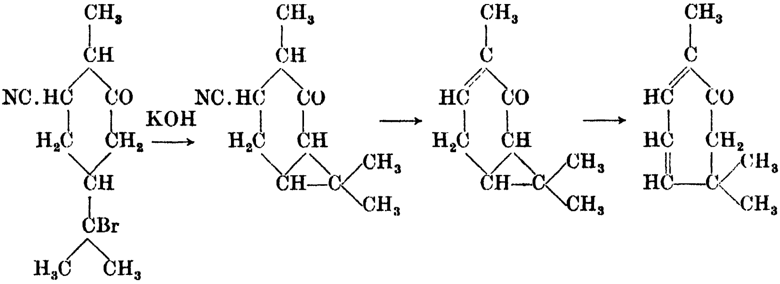
Carone does not react with sodium hydrogen sulphite or with the sodium derivative of ethyl cyanoacetate. When heated with an alcoholic solution of ammonium hydrogen sulphide under pressure at 145–150° it gives a substance, $(C_{10}H_{17})_2S_2$, b.p. 238–242°, the constitution of which has not been determined.[*] With hydrogen cyanide, carone gives an unstable *cyanohydrin*, which is reconverted into the parent ketone by alkali.[†]

---

[*] *Ber.* 1895, **28**, 641, 1596.

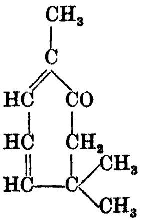
[†] Baeyer, *Ber.* 1896, **29**, 16.

d-*Cyanocarone* (XXXIV), m.p. 54–55°, α_D +298° (in alcohol), *semicarbazone*, m.p. 218–221°, has been described by Clarke and Lapworth,[‡] who prepared it by the action of alkali on *cyanodihydrocarvone hydrobromide* (XXXIII).[§] The presence of the *cyclo*propane ring in cyanocarone was proved by its oxidation with potassium permanganate to caronic acid. When warmed with alkali in the presence of ferrous hydroxide the nitrile is converted with loss of hydrogen cyanide into *eucarvone* (XXXVI), the unsaturated dicyclic ketone (XXXV), which must be the primary product of the reaction, being apparently unstable and immediately isomerising. The bearing of this reaction on the mechanism of the formation of eucarvone is discussed further on p. 90.



(XXXIII) (XXXIV) (XXXV) (XXXVI)

EUCARVONE



---

[*] Agostinelli, *Gazzetta*, 1913, **44**, 111.

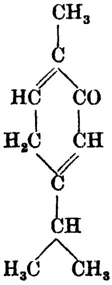
[†] Menon and Simonsen, *J. Ind. Inst. Sci.* 1927, **10A**, 5.

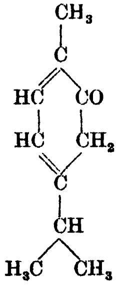
[‡] *J.C.S.* 1910, **97**, 12.

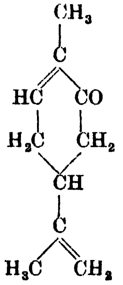
[§] Lapworth, *J.C.S.* 1906, **89**, 1826.

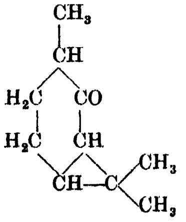
Although eucarvone, $C_{10}H_{14}O$, is a monocyclic ketone derived from carvone, it is conveniently considered here, since it was originally regarded as dicyclic and the determination of its constitution was directly dependent upon the determination of that of carone. Its occurrence in nature has only once been reported, when it was obtained by steam distillation of *Asarum Sieboldi* var. *seoulensis* Nakai.[*]

Contemporaneously with his experiments on the removal of hydrogen bromide from dihydrocarvone hydrobromide, which resulted in the preparation of carone,[†] Baeyer[‡] investigated the action of alkali on carvone hydrobromide, when an optically inactive ketone, $C_{10}H_{14}O$, "eucarvol", was obtained. At the time of these experiments carvone was considered to have formula (I) and eucarvol or eucarvone, as it was later called, was given (II).


(I)


(II)


(III)


(IV)

The subsequent proof that carvone had formula (III) and that carone was the dicyclic ketone (IV) naturally led Baeyer[§] to modify the formula for eucarvone, which he now regarded as the unsaturated dicyclic ketone (VI) from *carvone hydrobromide* (V) in a similar manner to carone from dihydrocarvone hydrobromide.

With carone, direct evidence of the presence of the *cyclo*propane ring was readily obtained by its oxidation to caronic acid (p. 78), but eucarvone, when oxidised under similar conditions, gave as-*dimethylsuccinic acid* (VII). This discrepancy

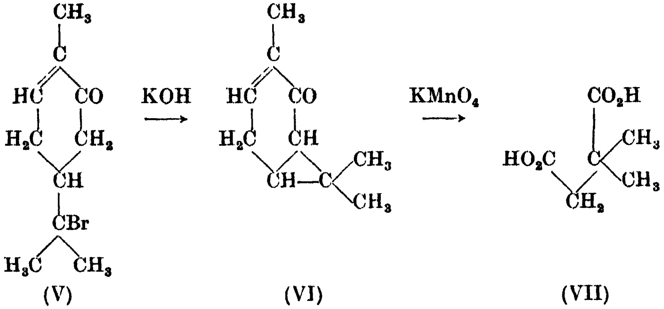
---

[*] Kaku, Kondo, Cho and Orita, *Keijo J. Med.* 1931, **2**, 566.

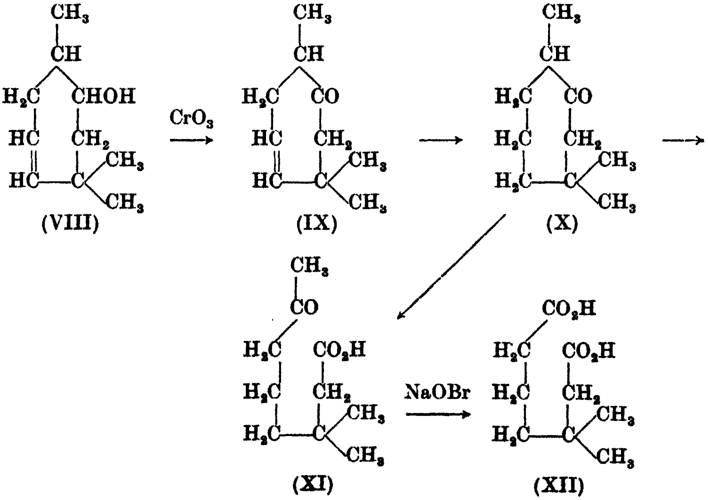
[†] *Ber.* 1894, **27**, 1915.

[‡] *Ibid.* p. 810.

[§] *Ibid.* 1898, **31**, 2067.



between the two ketones was ascribed by Baeyer to the instability of this ring in the unsaturated ketone, and in support of this he directed attention to the fact that, when eucarvone was reduced with sodium and alcohol, it gave an unsaturated secondary alcohol, *dihydroeucarveol*, $C_{10}H_{18}O$, from which an unsaturated ketone, *dihydroeucarvone*, $C_{10}H_{16}O$, could be prepared by oxidation with chromic acid. These two derivatives of eucarvone undoubtedly contained a *cyclo*heptene ring and Baeyer represented them by formulae (VIII) and (IX). The evidence for this was obtained in a somewhat indirect manner. *Dihydroeucarvoxime* gives with hydrogen iodide a crystalline hydroiodide, $C_{10}H_{18}ONI$, m.p. 161–162°, from which, by reduction with zinc



dust and alcoholic hydrochloric acid, an oxime can be prepared which on hydrolysis yields a saturated ketone, *tetrahydroeucarvone*, $C_{10}H_{18}O$. If dihydroeucarvone has formula (IX), the saturated ketone must be represented by (X). This was confirmed by its oxidation to the liquid *ketonic acid*, $C_{10}H_{18}O_3$ (XI), *semicarbazone*, m.p. 101–102°, from which by the action of sodium hypobromite *ββ-dimethylpimelic acid* (XII), m.p. 101–102·5°, was prepared.

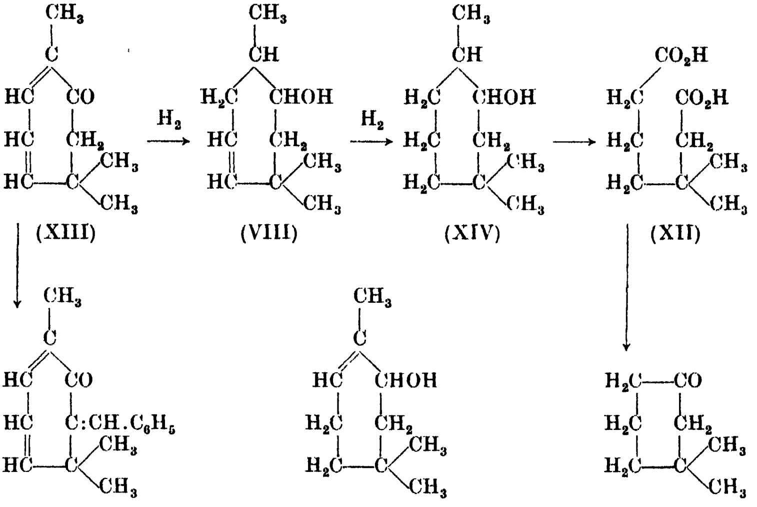
Whilst these experiments proved beyond question the presence of a seven-membered ring in dihydroeucarveol, dihydroeucarvone and tetrahydroeucarvone, many objections, fully recognised by Baeyer, could be urged against the dicyclic structure for eucarvone. Amongst the more important of these are (i) reduction would be expected to give, as is the case with carone (p. 80), derivatives of carvomenthone, (ii) oxidation should give caronic acid, and (iii) by the action of hydrogen chloride carvone hydrochloride should be obtained.

A reinvestigation of the properties of eucarvone by Wallach* furnished conclusive evidence that eucarvone, like its reduction products, contained a seven-membered ring, and he suggested formula (XIII). It will be observed that this represents the ketone as containing the group —CH_2—CO—, the presence of which was confirmed by the preparation of a *benzylidene* derivative (XVI). Wallach further showed that, when the ketone was reduced with sodium and alcohol, in addition to dihydroeucarveol (VIII), *tetrahydroeucarveol* (XIV) was also formed, which could be oxidised with chromic acid to tetrahydroeucarvone (X), identical with the ketone prepared indirectly by Baeyer from dihydroeucarvoxime. Incidentally Wallach confirmed the constitution assigned to the substituted pimelic acid (XII) by converting it, by distillation of the calcium salt, into 3:3-*dimethyl*cyclo*hexanone* (XV). The various reactions involved are shown in the scheme on p. 89.

It must be pointed out that no direct evidence of the position of the ethylenic linkage in dihydroeucarveol or dihydroeucarvone was provided either by the investigations of Baeyer or Wallach, and the alternative formula (XVII) was possible (see p. 89).

---

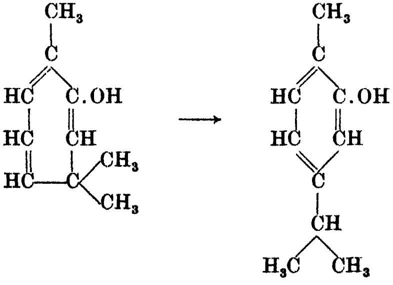
* *Annalen*, 1899, **305**, 242, 274; 1905, **339**, 94; *Ber.* 1896, **29**, 1600.



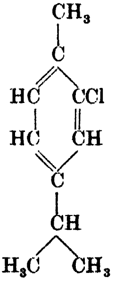
(XIII) (VIII) (XIV) (XII)

(XVI) (XVII) (XV)

The adoption of Wallach's formula explained *inter alia* (i) why the ketone, although prepared from an active hydrobromide, was always optically inactive, since it does not contain an asymmetric carbon atom, (ii) the very high molecular refraction, 46·72, in place of the calculated value, 43·72, for a dicyclic unsaturated ketone, and (iii) the formation of a hydroxylamino-oxime (see p. 94). The only important facts which could be urged against the formula were (i) the ready isomerisation of eucarvone to carvacrol (XIX), which probably takes place through the *enolic* form (XVIII)* of the ketone, and (ii) the



(XVIII) (XIX)



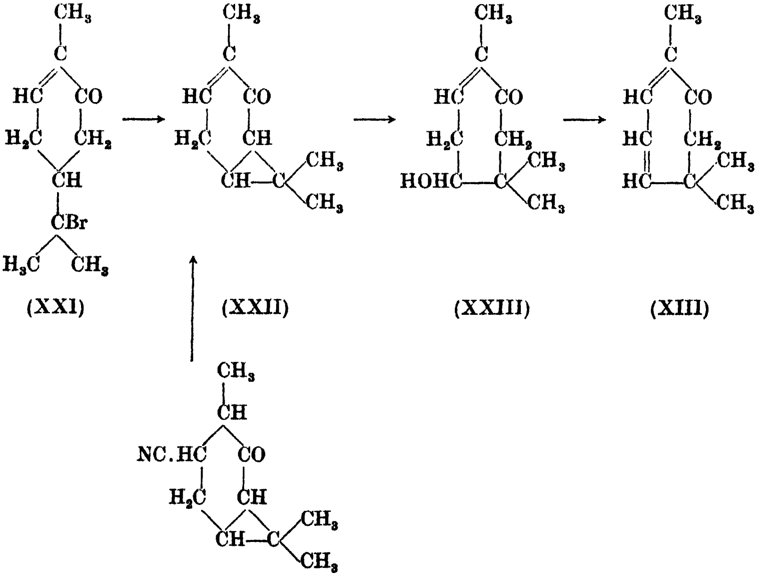
(XX)

---

* Baeyer, *Ber.* 1894, **27**, 812; compare Dormaar, *Rec. trav. chim.* 1904, **23**, 400.

formation of 2-*chloro*-p-*cymene* (XX) by the action of phosphorus pentachloride.[*]

To explain the formation of eucarvone from carvone hydrobromide (XXI) by the action of alkali Wallach suggested that, as was anticipated by Baeyer, the primary product of the reaction is the dicyclic ketone (XXII), which is, however, unstable and passes through the hydroxy-ketone (XXIII) into eucarvone. Confirmatory evidence of this view of the mechanism of the reaction was supplied by an investigation of Clarke and Lapworth,[†] who showed that, when cyanocarone (XXIV) was treated with alkali in the presence of ferrous hydroxide, eucarvone was formed. In this case there can be no doubt that the dicyclic ketone (XXII) must be the primary product of the reaction.


(XXI) (XXII) (XXIII) (XIII)

(XXIV)

Eucarvone is a colourless oil with an odour resembling that of menthone. The following constants were observed by Auwers[‡] for the ketone purified through its semicarbazone: b.p. 88°/10 mm.,

---

[*] Klages and Kraith, *Ber.* 1899, **32**, 258.

[†] *J.C.S.* 1910, **97**, 15.

[‡] *Annalen*, 1918, **415**, 164.

$d_{4^\circ}^{20^\circ}$ 0·9490, $n_D^{20^\circ}$ 1·5087. The molecular refraction shows an exaltation of + 1·35 units, which, as noted by Auwers and Eisenlohr,[*] is remarkably low, the ketone resembling in this respect ionone. The ketone is isomerised when distilled under the ordinary pressure. The heat of combustion has been determined by Roth and Östling[†] and found to be 1373·1 kg.-cals. The absorption spectrum is typical of a conjugated dienone.[‡]

Eucarvone can be identified by the preparation of the *semicarbazone*, m.p. 183–185°,[§] or the 2:4-*dinitrophenylhydrazone*, m.p. 152–153°,[‖] whilst, when it is mixed with a concentrated methyl alcoholic solution of potassium hydroxide, it gives a highly characteristic deep blue colour, which is discharged on dilution with water.[¶] With maleic anhydride it gives an *adduct*, m.p. 165–167°.[**] Eucarvone is somewhat unstable and when boiled for one hour is completely isomerised to carvacrol.

By the catalytic hydrogenation of eucarvone in the presence of palladium, Wallach[††] prepared *tetrahydroeucarvone*, b.p. 208–209°, d^{20° 0·9063, $n_D^{20^\circ}$ 1·4554, *semicarbazone*, m.p. 201° and 161–163°, *nitroso*-derivative, m.p. 104–105°. This ketone is now therefore readily accessible; previously it could only be obtained by the laborious process referred to above. As mentioned, reduction of eucarvone with sodium and alcohol gives a mixture of α-*dihydroeucarveol* and *tetrahydroeucarveol*.[‡‡] α-Dihydroeucarveol, which for the reasons given below must have formula (VIII), is a viscid oil, b.p. 216°, 114°/16 mm., d^{20° 0·929, $n_D^{20^\circ}$ 1·4758, *phenylurethane*, m.p. 61–63°, and gives on oxidation with chromic acid α-*dihydroeucarvone* (IX),[§§] b.p. 202–203°, 86–87°/16 mm., $d_{4^\circ}^{20^\circ}$ 0·9222, $n_D^{20^\circ}$ 1·4697, *semicarbazone*, m.p. 189–191°, *bis-nitroso*-derivative, m.p. 121–124°;[‖‖] the oxime is an oil.

By the reduction of eucarvoxime (XXV) with hydrogen in the presence of palladium, Wallach and Klein[¶¶] prepared a crystalline β-*dihydroeucarvoxime* (XXVI), m.p. 122–123°, from which on hydrolysis an isomeric β-*dihydroeucarvone*, b.p. 213–214°,

---

[*] *J. pr. Chem.* 1911 [ii], **84**, 80.

[†] *Ber.* 1913, **46**, 324.

[‡] Gillam and West, *J.C.S.* 1942, p. 485.

[§] Baeyer, *Ber.* 1894, **27**, 1923.

[‖] West, *J.C.S.* 1940, p. 1162.

[¶] Baeyer, *Ber.* 1894, **27**, 812.

[**] West, *loc. cit.*

[††] *Annalen*, 1911, **381**, 67; 1914, **403**, 87.

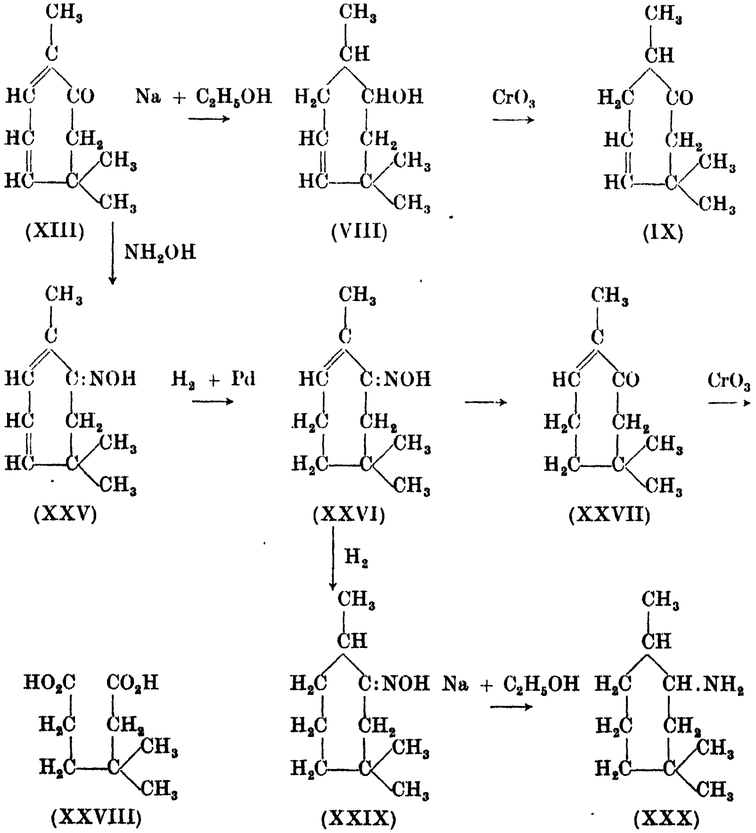
[‡‡] Baeyer, *Ber.* 1894, **27**, 1922; Wallach and Koehler, *Annalen*, 1905, **339**, 102.

[§§] Baeyer, *Ber.* 1894, **27**, 1922; Klages and Kraith, *ibid.* 1899, **32**, 2563.

[‖‖] Baeyer, *ibid.* 1895, **28**, 646.

[¶¶] *Annalen*, 1914, **403**, 87.

$d^{21°}$ 0·9325, $n_D^{21°}$ 1·4790, *semicarbazone*, m.p. 202°, was obtained. This ketone differed from the isomeric dihydro-ketone in not giving a nitroso-derivative, but it formed a *nitrosochloride*, m.p. 95°. The two isomeric dihydroeucarvones differ in the position of the ethylenic linkage, and the constitution of the β-ketone (XXVII) is proved by its oxidation to *ββ-dimethyladipic acid* (XXVIII), m.p. 80°. These structures are confirmed by recent observations of the absorption spectra;* the β-ketone, in which the ethylenic linkage is conjugated with the carbonyl group, shows the expected absorption at λ 2395 A., which is not exhibited by the isomer. There are therefore the two following schemes



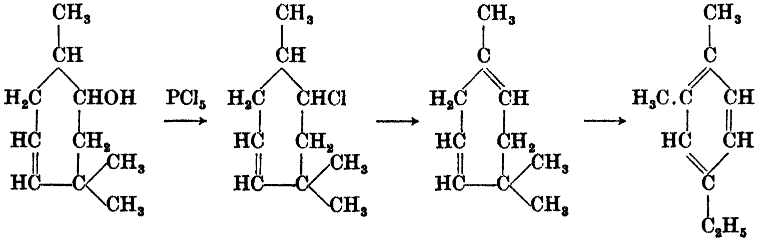
---

* Gillam and West, *J.C.S.* 1942, p. 485.

for the preparation of the isomeric dihydroeucarvones; β-dihydroeucarveol has not been described.

Additional evidence in support of the structural isomerism of the two dihydroeucarvones was furnished by the catalytic hydrogenation of β-dihydroeucarvoxime to *tetrahydroeucarvoxime* (XXIX), m.p. 56–57°, which when reduced with sodium and alcohol gives tetrahydroeucarvylamine (XXX), b.p. 208·5°, $d^{21°}$ 0·8680, $n_D^{21°}$ 1·4665, *acetyl* derivative, m.p. 110·5°, *benzoyl* derivative, m.p. 168°. This base contains two asymmetric carbon atoms, but apparently only one externally compensated form has been isolated. By reduction of eucarvone with zinc dust in alkaline media three isomeric *pinacones*, $C_{20}H_{30}O_2$, are formed, the constitutions of which have been discussed by Wallach.*

No crystalline derivatives of eucarvone with the halogens or halogen acids have been described, although Wallach† studied the bromination of the dihydroeucarvones. When eucarvone in light petroleum solution is treated with phosphorus pentachloride it yields a *chloro*-derivative, which by the action of quinoline passes into 2-chloro-*p*-cymene.‡ The conversion of eucarvone into derivatives of benzene was carried out by Baeyer in an interesting series of reactions.§ By the action of phosphorus pentachloride on α-dihydroeucarveol (VIII) a *chloride*‖ was prepared, which was not homogeneous, distilled about 100–110°/29 mm. and consisted essentially of the substance (XXXI). When the chloride was treated with quinoline a *hydrocarbon*, *euterpene*, b.p. 161–165°, was obtained, which is probably the *cyclo*heptadiene hydrocarbon (XXXII), although the constitution



(VIII) (XXXI) (XXXII) (XXXIII)

---

* *Annalen*, 1914, **403**, 102.

† *Ibid.* 1919, **418**, 53.

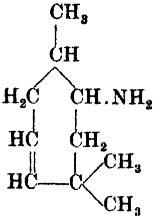
‡ Klages and Kraith, *Ber.* 1899, **32**, 2558.

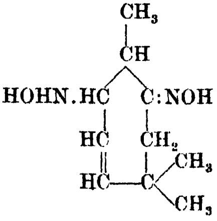
§ *Ber.* 1898, **31**, 2077.

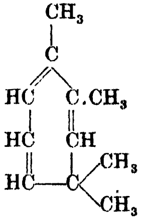
‖ Klages and Kraith (*Ber.* 1899, **32**, 2561) give the b.p. 85°/20 mm., $d^{18°}$ 0·935, n_D 1·4617.

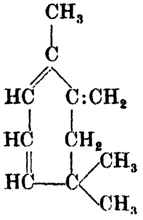
has not been rigidly proved. Oxidation with potassium permanganate gives *as*-dimethylsuccinic acid, whilst degradation by the Baeyer-Villiger method of exhaustive bromination yields 1:2-*dimethyl*-4-*ethylbenzene* (XXXIII).

Eucarvoxime, m.p. 106°, was described by Baeyer[*] and by Wallach.[†] Although it can be hydrolysed to the parent ketone it is somewhat stable to hydrolytic agents. On reduction with sodium and alcohol it yields a mixture of *α-dihydroeucarvylamine* (XXXIV), b.p. 116–117°/40 mm., *phenylurethane*, m.p. 142° and *tetrahydroeucarvylamine* (see p. 93).


(XXXIV)


(XXXV)


(XXXVI)


(XXXVII)

Like the tetrahydro-base, the dihydro-base is theoretically capable of existing in two externally compensated forms.

When eucarvone is treated with an excess of hydroxylamine it yields a *hydroxylamino-oxime* (XXXV),[‡] which melts at 141–142° and gives a hydrogen oxalate, m.p. 198°.

Eucarvone does not react with sodium hydrogen sulphite but, as was mentioned on p. 88, it reacts with benzaldehyde in the presence of sodium ethoxide to give a *benzylidene* derivative crystallising in yellow prisms, m.p. 112–113°. At the same time a colourless substance, $C_{24}H_{24}O_2$, m.p. 193–194°, is formed, the constitution of which has not been determined.[§] The action of methyl magnesium iodide on eucarvone has been investigated by Rupe and Kerkovius,[‖] who obtained a *hydrocarbon*, $C_{11}H_{16}$, b.p. 67–68°/11 mm., $d^{20°}$ 0·8687, $n_D^{20°}$ 1·5066. The constitution of this has not been established, but it is not improbable that it is a mixture of the two substances represented by (XXXVI) and (XXXVII).

[*] *Ber.* 1894, **27**, 813.

[†] *Annalen*, 1899, **305**, 239.

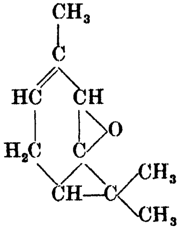
[‡] Harries, *Annalen*, 1904, **330**, 275.

[§] Wallach, *Ber.* 1896, **29**, 1600; *Annalen*, 1899, **305**, 242, 275.

[‖] *Ber.* 1911, **44**, 2703.

C. OXIDE

Δ³-CARENE-5:6-EPOXIDE



A constituent, $C_{10}H_{14}O$, of the essential oil derived from the leaves and terminal branchlets of *Zieria Smithii*, which grows in New South Wales, Queensland and Victoria, has been shown by Penfold and Simonsen* to be a derivative of Δ³-carene, namely l-Δ³-*carene*-5:6-*epoxide* (I). This somewhat unusual tricyclic structure is based upon the following evidence.

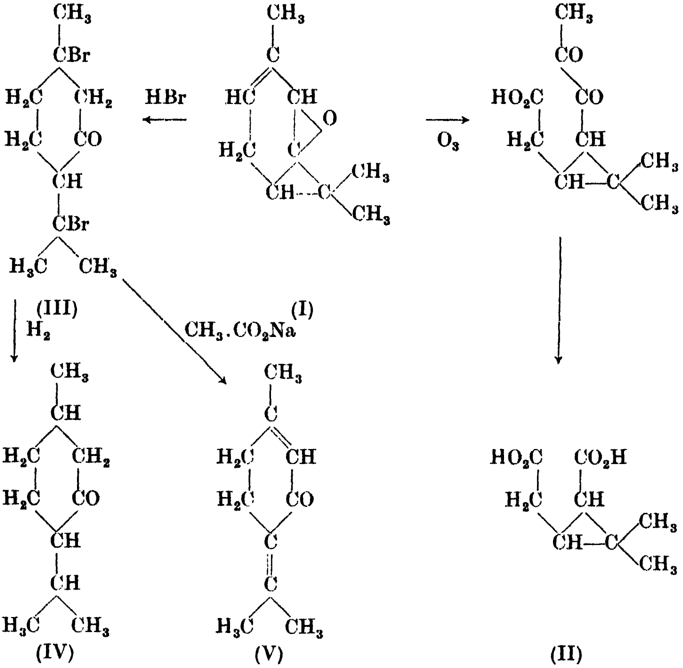
On ozonolysis cis-*homocaronic acid* (II) (compare p. 68) was obtained, thus affording proof of the presence of the *cyclo*propane ring, whilst on treatment with hydrogen bromide dl-1:8-*dibromo*-p-*menthan*-3-*one* (III), m.p. 74°, was formed. This reaction is comparable with the conversion of Δ³- and Δ⁴-carenes into dipentene dihydrochloride by the action of hydrogen chloride (compare pp. 66, 76), the ring fission in this case being accompanied by the isomerisation of the epoxide to a ketone. This facile isomerisation to carbonyl derivatives is discussed further below. The structure of the dibromomenthone, which had not been described previously, was established by its hydrogenation to dl-*menthone* (IV) and by its conversion on digestion in acetic acid solution with sodium acetate to $\Delta^{1:4(8)}$-p-*menthadien*-3-*one* (piperitenone) (V), which occurs in the oil from *Mentha Pulegium* var. *Villosa* Benth.† (compare Vol. I, p. 409).

Whilst these reactions are in accord with the suggested structure (I), rigid proof of the presence of the ethylenic linkage and of the epoxide ring could not be obtained. Catalytic hydrogenation was accompanied by ring fission as is commonly the case with

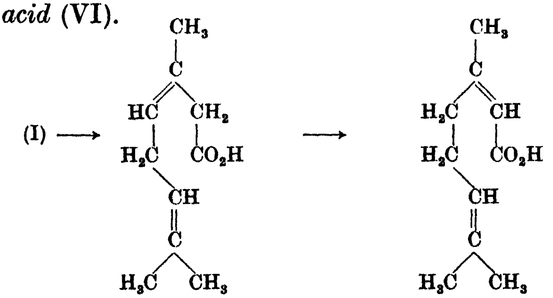
---

* *J.C.S.* 1939, p. 1496.

† Naves, *Helv. Chim. Acta*, 1942, **25**, 732.



dicyclic substances containing the *cyclo*propane ring.[*] Nor was it found possible to prepare a glycol, since the epoxide, if heated with water at 150° or digested with dilute aqueous alkali, gave *geranic acid* (VI).

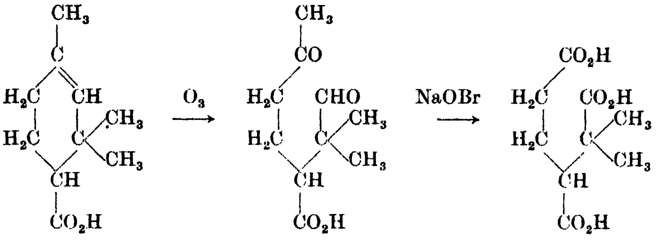


(VI)

If, however, the epoxide was allowed to stand in the cold with ethyl alcoholic potassium hydroxide for 14 days the reaction proceeded in a completely different manner with the formation of a crystalline *acid*, $C_{10}H_{14}O_2$, m.p. 83°. This acid was shown by Penfold and Simonsen* to be 1:3:3-*trimethyl*-Δ^1-*cyclo*hexene-4-*carboxylic acid* (VII), since it gave, on ozonolysis followed by further oxidation with sodium hypobromite, *β-methylpentane-βγε-tricarboxylic acid* (VIII), m.p. 153°.

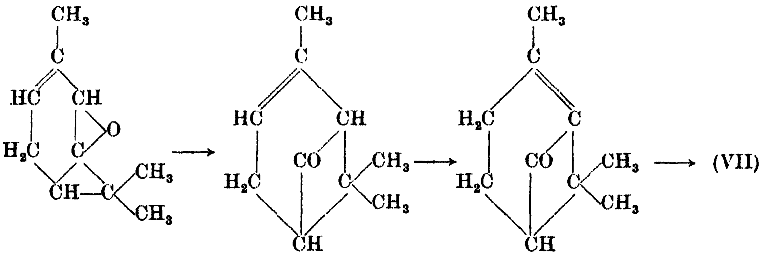
---

[*] Compare Iyer and Simonsen, *J.C.S.* 1926, p. 2049; Short and Read, *ibid.* 1938, p. 2016; 1939, p. 1040.



(VII) (VIII)

The formation of the *cyclo*hexene acid is obviously connected with the marked tendency shown by the epoxide to isomerise to ketones, and it is most probable that the reaction proceeds in accordance with the scheme set out below:



(I) (IX)

l-Δ^3-Carene-5:6-epoxide is a colourless mobile oil with a pleasant odour, b.p. 83–85°/14 mm., $d_{25^\circ}^{25^\circ}$ 0·9454, $n_D^{25^\circ}$ 1·4792, $[\alpha]_{5461}$ − 88°. The absorption spectrum was examined by Gillam† and this, whilst definitely excluding the presence of the chromophoric system $>C:\overset{|}{C}.\underset{|}{C}:O$, does not definitely exclude the presence of an isolated carbonyl group. The epoxide can be most readily characterised by the preparation of the dibromomenthone, m.p. 74°, referred to on p. 95 or the related *dichloride*, m.p. 72°, obtained by the action of hydrogen chloride.

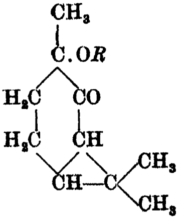
---

* *J.C.S.* 1942, p. 206.

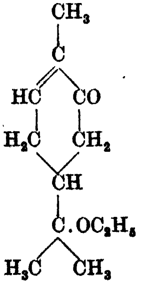
† *J.C.S.* 1939, p. 1499.

Whilst the epoxide distilled without decomposition under diminished pressure, it developed a deep yellow colour when distilled at the ordinary pressure or if it was heated for a short time at 160–170°. The oil so obtained reacted immediately with carbonyl reagents yielding two *semicarbazones*, m.p. 221–223° and 183–185°, respectively, and a very sparingly soluble purple 2:4-*dinitrophenylhydrazone*, m.p. 218–220°, derived from a ketone of the formula $C_{10}H_{14}O$. The structure of the ketone, from which these derivatives were formed, was not determined, but it is possible that it was represented by (IX).

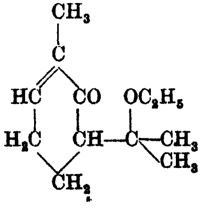
Slow isomerisation of the epoxide occurs also on treatment with carbonyl reagents. With 2:4-dinitrophenylhydrazine sulphate in aqueous solution a yellow 2:4-*dinitrophenylhydrazone*, m.p. 143–144°, of a hydroxy-ketone, $C_{10}H_{16}O_2$, was obtained, whilst in alcoholic solution two 2:4-*dinitrophenylhydrazones*, one crystallising in garnet prisms, m.p. 192–193°, and the second in orange yellow needles, m.p. 165–166°, derived from an ethoxy-ketone, $C_{12}H_{20}O_2$, are formed. Whilst the simplest explanation of the formation of these derivatives would be that they are derived from the epoxide by isomerisation to an unsaturated ketone, accompanied by ring fission with the addition of water and alcohol respectively to give either hydroxy (or ethoxy)-*m*- or *p*-menthenones, the marked difference in their colour would suggest that this explanation is inadequate. A more probable explanation is that the yellow 2:4-dinitrophenylhydrazones are derived from the ketone represented by (X), where *R* is either



(X)



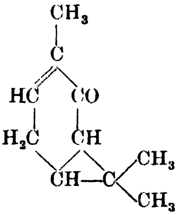
(XI)



(XII)

hydrogen or ethyl, whilst the garnet 2:4-dinitrophenylhydrazone is a derivative of either (XI) or (XII).

With semicarbazide acetate in methyl alcoholic solution a mixture of semicarbazones resulted from which, on crystallisation, fractions were obtained not differing appreciably in melting-point, *ca.* 192°, but showing a marked difference in their rotatory power, $[\alpha]_{5461}$ $-95°$ to $-70°$ (in pyridine). It would appear not improbable that these *semicarbazones* are derived from the carenone (XIII), which, although unstable in the free state (compare p. 90), may be stable in the form of derivatives. The varying rotatory power may have been due in part to the fact that the semicarbazone was not stereochemically homogeneous.


(XIII)

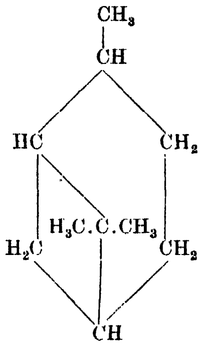
This would be anticipated, since isomerisation of the epoxide involves one of the asymmetric centres. Some support for this view was furnished by the fact that treatment of the semicarbazone with 2:4-dinitrophenylhydrazine sulphate in ethyl alcoholic solution gave a mixture of the two 2:4-dinitrophenylhydrazones, m.p. 192–193° and 165–166°, referred to above. Hydrolysis of the crude semicarbazone with either oxalic or phthalic acid gave a mixture of ketones, one of which was piperitenone (V) (p. 96). A fraction of lower boiling-point contained a ketone, $C_7H_{10}O$, 2:4-*dinitrophenylhydrazone*, m.p. 176–177°, which was not identified.

CHAPTER III

PINANE AND ITS DERIVATIVES

A. HYDROCARBONS

PINANE

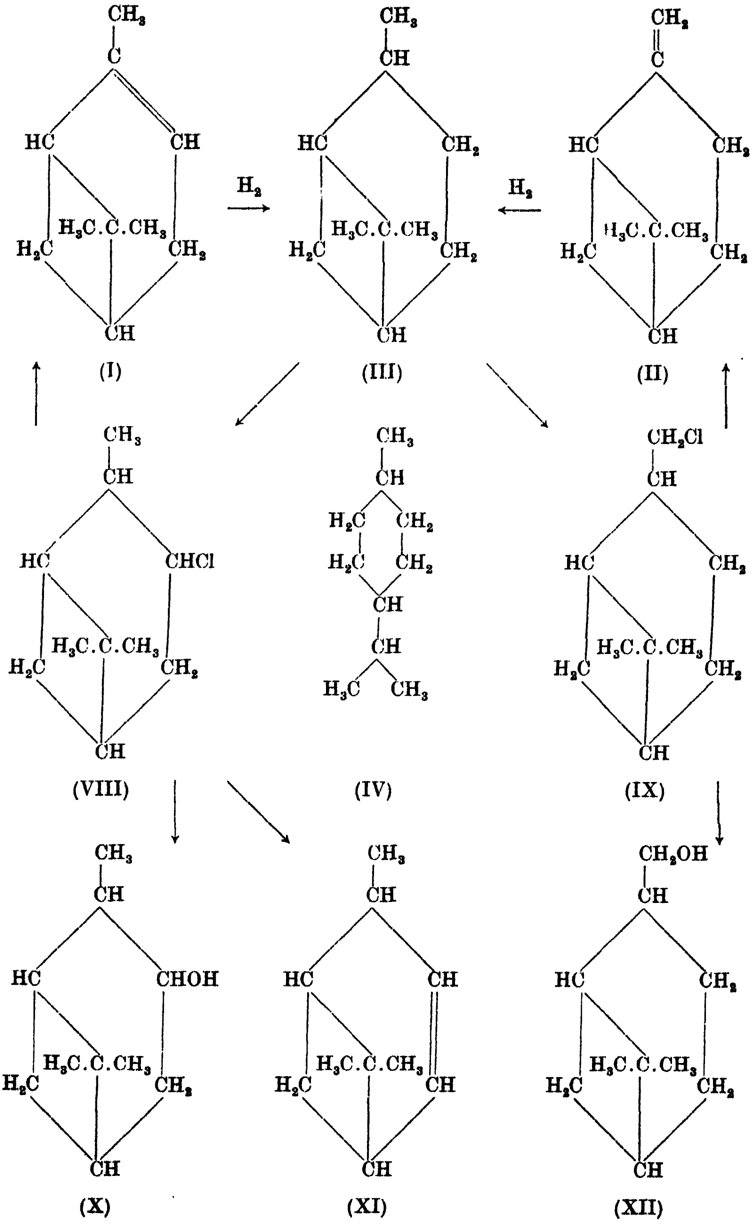


Addition of a molecule of hydrogen to the ethylenic linkage present in either α-pinene (I) or β-pinene (II) should, in the absence of isomerisation, lead to the formation of the saturated dicyclic hydrocarbon, *pinane* (III). As is mentioned on p. 135, the early experiments on the reduction of pinene (a mixture of α- and β-pinenes) involved the use of acidic reducing agents and high temperatures, so that the product of the reaction consisted essentially of p-*menthane* (IV). With the introduction of the catalytic methods of hydrogenation, it has, however, become possible to prepare pinane free from isomerides.

The first experiments on the catalytic hydrogenation of α-pinene were made by Sabatier and Senderens,* who reduced *l*-α-pinene at 170–180° using a nickel catalyst. They obtained a saturated hydrocarbon, b.p. 166°, $d_{4^\circ}^{0^\circ}$ 0·862, which they assumed to be pinane, although they furnished no evidence in support of this structure. Subsequently both *d*- and *l*-α-pinenes were reduced by other investigators, either by the Sabatier-Senderens process, or at ordinary temperature, using a platinum or palladium

---

* *Compt. rend.* 1901, **132**, 1256.


(I)
H_2
(III)
H_2
(II)
(VIII)
(IV)
(IX)
(X)
(XI)
(XII)

catalyst.[*] Pinane was also prepared by the hydrogenation of β-pinene,[†] from *pinocamphonehydrazone* (p. 232) by Kishner's method, from d-*verbanonehydrazone* (p. 236) by the action of sodium ethoxide at 140–160°[‡] and from *pinocamphone semicarbazone* by Wolff's reaction.[§] Whilst the boiling-points of the hydrocarbons, so prepared, were approximately the same as that observed by Sabatier and Senderens, very marked differences occurred in the densities and refractive indices.[‖] To account for these differences, it was suggested that possibly reduction of the ethylenic linkage was accompanied, at any rate to some extent, by ring fission, and that the hydrocarbon, although possessing a constant boiling-point, was actually a mixture of pinane, *p*-menthane and possibly also *o*-menthane.

In an admirable paper by Lipp[¶] an explanation was given which fully accounts for these anomalies. He pointed out that it had not apparently been fully appreciated that, on reduction of either α- or β-pinene, the *cis*- and *trans*-modifications of pinane might be formed. Now it is known from the investigations of Auwers[**] and Skita[††] that the *cis*- and *trans*-forms of a substance differ in density and refractive index, the *trans*- having the lower density and refractive index. Herein Lipp found an explanation of the divergent results of previous investigators, which he confirmed by his own experiments, whilst at the same time he advanced experimental evidence to show that the hydrocarbon obtained was actually pinane.

When *l*-α-pinene ($[\alpha]_D$ −38·08°) was reduced by the Sabatier-Senderens process with a nickel catalyst at 220–230°, *trans*-*l*-pinane, b.p. 162–164°/720 mm., $d_{4°}^{17\cdot5°}$ 0·8519, $n_D^{17\cdot5°}$ 1·4595, $[\alpha]_D$ −16·1°, was obtained. By reduction in the presence of platinum black at the ordinary temperature *cis*-*l*-pinane, b.p. 164·8–165·8°/716 mm., $d_{4°}^{20°}$ 0·8562, $n_D^{20°}$ 1·4624, $[\alpha]_D$ −18·9°, was prepared. From *d*-α-pinene ($[\alpha]_D$ +47·5°), *cis*-*d*-pinane, b.p.

---

[*] Sabatier and Maihle, *Bull. Soc. chim.* 1906 [iii], **36**, 615; Vavon, *Compt. rend.* 1909, **149**, 998; *Bull. Soc. chim.* 1911 [iv], **9**, 256; Zelinski, *Ber.* 1911, **44**, 2784; Nametkin and Jarzev, *J. Russ. Phys. Chem. Soc.* 1920, **51**, 147; *Ber.* 1923, **56**, 832.

[†] Vavon, *Compt. rend.* 1910, **150**, 1127.

[‡] *Annalen*, 1924, **439**, 36.

[§] Nametkin and Jarzev, *Ber.* 1923, **56**, 832.

[‖] The optical rotatory power naturally varied, both in sign and magnitude, with that of the α- or β-pinene reduced.

[¶] *Ber.* 1923, **56**, 2098.

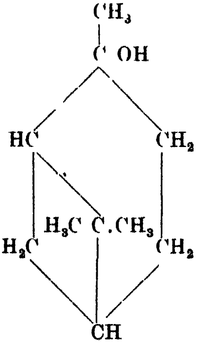
[**] *Annalen*, 1919, **420**, 91.

[††] *Ber.* 1920, **53**, 1792.

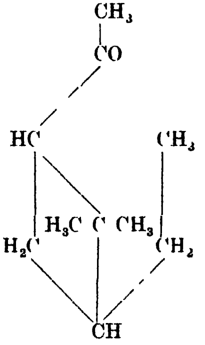
163–164°/720 mm., $d_{4^\circ}^{20^\circ}$ 0·8566, $n_D^{20^\circ}$ 1·4624, $[\alpha]_D$ +23·08°, was prepared in a similar manner. The molecular refraction of these three hydrocarbons was found to be the same, 44·36, 44·35, 44·37, showing an exaltation of approximately 0·4 unit.

There is of course no evidence that the *cis*- and *trans*-pinanes were the pure isomerides, and this is indeed improbable, but direct proof of their constitution was furnished by their oxidation with potassium permanganate to *methylnopinol* (V), m.p. 79°. This alcohol is probably a stereoisomeride of the substance, m.p. 58–59°, prepared by Wallach[*] by the action of methyl magnesium iodide on nopinone. On hydration with sulphuric acid it gives terpin hydrate, whilst, by the further action of potassium permanganate, pinonic acid is obtained.

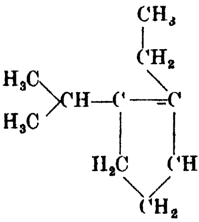
It has been suggested by Zelinski and Lewina[†] that *β*-pinene does not give pinane on catalytic hydrogenation, the catalyst used being palladium deposited on charcoal and the temperature 170–175°. This has been shown by Lipp[‡] to be incorrect. *l*-*β*-Pinene gives, on catalytic hydrogenation in the presence of platinum black, *cis*-*l*-pinane identical in all respects with that prepared from *l*-α-pinene. If, however, Zelinski and Lewina's method of hydrogenation be adopted, a much more profound change occurs and the product obtained is a mixture, the constituents of which have, however, not been identified.



(V)



(VI)



(VII)

Schmidt[§] has recently obtained the *cis*- and *trans*-pinanes by hydrogenation of the stereoisomeric forms of δ-pinene.

---

[*] *Annalen*, 1907, **356**, 239.

[†] *Ber.* 1929, **62**, 339.

[‡] *Ibid.* 1930, **63**, 412.

[§] *Chem. Ber.* 1947, **80**, 520.

Since α-pinene, pinocamphone, and verbanone have recently been obtained synthetically (pp. 128, 228, 235) the total synthesis of pinane may also be considered to have been accomplished.

The rotatory power of pinane in different solvents has been measured by Rule and Chambers.[*]

Pinane is remarkably stable both to oxidising agents and mineral acids. It is only very slightly attacked by hydrogen bromide at 230°, whilst on reduction with hydriodic acid and red phosphorus it yields a hydrocarbon, $C_{10}H_{20}$, b.p. 160–165°, $d_{4^\circ}^{20^\circ}$ 0·8019, $n_D^{20^\circ}$ 1·4393, which is not homogeneous, but probably consists essentially of *p*-menthane. According to Shochet[†] the oxidation of *d*-pinane by air at 110° gives 4-*acetyl*-1:1-*dimethyl*-2-*ethyl*cyclo*butane* (VI). Pyrolysis of the hydrocarbon gives a complex mixture of acyclic and monocyclic dihydroterpenes,[‡] whilst when heated under pressure with magnesium chloride solution it is isomerised to 1-*ethyl*-2-iso*propyl*cyclo*pentene* (VII).[§] When dehydrogenated over a platinum catalyst it gives *o*- and *p*-cymene, and also 1:2:3- and 1:2:4-trimethylbenzenes.[‖]

By the action of chlorine on *d*-pinane, 1-2-*chloropinane* (VIII), b.p. 57°/2·5 mm., $[\alpha]_D$ −6°; d-7-*chloropinane* (IX), b.p. 66°/2·5 mm., $[\alpha]_D$ +10°; and a *dichloropinane*, b.p. 102°/2·5 mm., $[\alpha]_D$ −12°, are obtained.[¶] The 2-chloro-compound may be converted *via* the acetate or Grignard derivative into l-*pinocampheol* (X), m.p. 58–59° (see p. 101), whilst treatment with potassium phenoxide results in the loss of hydrogen chloride and the formation of α-pinene (I), together with some δ-*pinene* (XI).[**] Similarly, from 7-chloropinane, *dihydromyrtenol* (*myrtanol*) (XII) and β-pinene (II) are obtained; this amounts to an indirect synthesis of the latter hydrocarbon.

2-*Bromopinane* has m.p. 70–72°, and shows the same reactions as the 2-chloro-compound.

---

[*] *J.C.S.* 1937, p. 151.

[†] *Bull. Soc. chim. Belg.* 1935, **44**, 387.

[‡] Rummelsburg, *J. Amer. C.S.* 1944, **66**, 1718.

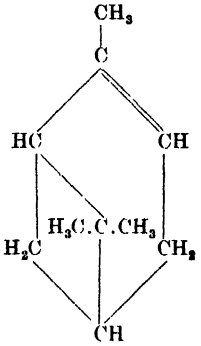
[§] Ipatiev and Pines, *ibid.* 1945, **67**, 1931.

[‖] Olberg, Pines and Ipatiev, *ibid.* 1948, **70**, 533; compare Linstead, Michaelis and Thomas, *J.C.S.* 1940, p. 1139.

[¶] Bonnet, *Bull. Inst. Pin*, 1938, pp. 217, 241; 1939, p. 1; Gandini, *Gazzetta*, 1940, **70**, 254.

[**] According to Treibs (*Annalen*, 1947, **558**, 136) δ-pinene can be purified by treatment with hydrogen chloride, with which, unlike α-pinene, it does not react. Pure δ-pinene has $\alpha_D^{20^\circ}$ −78°, $d_{4^\circ}^{20^\circ}$ 0·8647, $n_D^{20^\circ}$ 1·4661. A dextrorotatory form, α_D +51°, has been described by Schmidt (*Chem. Ber.* 1947, **80**, 520).

α-*PINENE*



Pinene must be regarded as the most important member of the terpene hydrocarbons, and it occurs very widely distributed in nature. It is present in the majority of essential oils derived from the Coniferae and it is the principal constituent* of oil of turpentine, which has been known from very early times. According to Flückiger† the name turpentine was given originally to the oil prepared from the oleo-resin of *Pistacia Terebinthus* L., and was probably first prepared in Persia, since the word "Termentin" or "Turmentin" is, according to Flückiger, Persian. The date of the introduction of the oil into the West does not appear to be known, but it is referred to in the literature of the thirteenth century, its valuable properties as a solvent being early recognised.

The designation, *pinene*, was given by Wallach‡ to the hydrocarbon fraction, b.p. 155–165°, of oil of turpentine, which had previously been known by a great variety of names, *inter al.*, terebenthine, australene, eucalyptene, olibanene, etc. This name was selected to indicate its association with the various species of *Pinus*, in which it is so largely found. In view of the facility with which turpentine could be obtained, its reactions have been investigated from a very early date and it is only possible here to summarise the more important researches. The first analysis of pinene was made by Lavoisier, but the correct composition,

---

* Gildemeister and Hoffmann, *Die Ätherischen Öle*, 1928, 1, 342.

† *Die Pharmakognosie*, 1883, p. 66.

‡ *Annalen*, 1885, 227, 300.

C_5H_8, was determined by Labilliardière,[*] Biot a few years previously (1815) having made the fundamental observation that French oil of turpentine was optically active and laevorotatory. Although during the following years a number of reactions of pinene were studied and crystalline "pinene hydrochloride", artificial camphor, prepared, the next important advance was due to Dumas,[†] who determined the molecular weight and showed the correct formula to be $C_{10}H_{16}$. In the next two decades little progress was made in the determination of the constitution of the hydrocarbon. It was observed that when pinene was treated with hydrogen chloride, in addition to "pinene hydrochloride", a dihydrochloride $C_{10}H_{16}$, 2HCl, identical with that prepared from limonene, was formed,[‡] whilst Berthelot[§] showed that when heated at 250–300° under pressure it was isomerised to hydrocarbons having a higher boiling-point. Some years later, Berthelot[||] made the very important observation that "pinene hydrochloride" could be converted into a crystalline hydrocarbon, camphene, and he recognised that pinene and camphene differed in structure.[¶] Amongst other derivatives prepared and studied during this period were dipentene dihydrochloride, terpin hydrate and sobrerol. A number of experiments on the oxidation of the hydrocarbon[**] were also carried out, but they did not yield results giving any clue to its constitution. Its relationship, however, to the aromatic hydrocarbons was established by the experiments of Barbier,[††] Oppenheim[‡‡] and Kekule,[§§] who showed that it could be converted into a methylpropylbenzene, but it was only many years later that Widmann[||||] actually proved this to be *p*-cymene.

In 1875, Tilden[¶¶] prepared pinene nitrosochloride (p. 178) and a few years later (cf. Vol. I, p. 144) he suggested that the terpenes could be divided into three main classes: (i) the turpentines, b.p.

---

[*] *J. Pharm. Chim.* 1818 [ii], **4**, 5.

[†] *Annalen*, 1833, **6**, 250.

[‡] *Inter al.*, Blanchet and Sell, *Annalen*, 1833, **6**, 271; Dumas, *ibid.* 1834, **9**, 56; Berthelot, *Ann. Chim.* 1854 [iii], **40**, 5, 31; *Annalen*, 1852, **84**, 350; List, *ibid.* 1848, **67**, 362; Deville, 1849, **71**, 351.

[§] *Annalen*, 1853, **88**, 342.

[||] *Ibid.* 1858, **110**, 367.

[¶] *Compt. rend.* 1862, **55**, 496, 544.

[**] *Inter al.*, Schönbein, *J. pr. Chem.* 1851 [i], **52**, 135; **53**, 65; **54**, 74; 1855 [i], **66**, 272 [i], **75**, 80; Chautard, *Annalen*, 1853, **88**, 340.

[††] *Compt. rend.* 1872, **74**, 194.

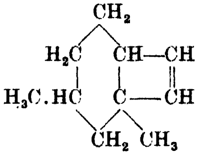
[‡‡] *Ber.* 1872, **5**, 94.

[§§] *Ibid.* 1873, **6**, 439.

[||||] *Ibid.* 1891, **24**, 439.

[¶¶] *J.C.S.* 1875, **28**, 514.

155–165°, (ii) the citrenes, b.p. 170–180°, and (iii) sylvestrene. It will be observed that this is actually a division into dicyclic and monocyclic terpenes. The chief value of the classification lay in the fact that it recognised for the first time that the number of terpenes was not unlimited. Other classifications were proposed at this time, but they were all superseded as knowledge of the chemistry of the various members of the terpene series developed. (Although Oppenheim and Kekule[*] had suggested that pinene was a derivative of dihydrocymene, and Armstrong[†] had actually put forward a dicyclic structure (I), the first systematic attempts to explain the reactions of the hydrocarbon were due to Wallach. Taking advantage of Tilden's important discovery of the nitrosochlorides, Wallach had in 1883 commenced a detailed study of the terpenes. On evidence which will be summarised in the sequel, he came to the conclusion that pinene contained only one ethylenic linkage, since it gave with hydrogen chloride a *monohydrochloride*, the *dihydrochloride* being a secondary product. He regarded pinol and pinol hydrate (sobrerol) (Vol. I, p. 436) as primary oxidation products, and he emphasised the importance of a determination of their constitution for the elucidation of that of pinene. In two memoirs published in 1887,[‡] he advanced the very important suggestion that the terpenes in general might be regarded as polymerisation products of the pentene, *isoprene*, C_5H_8, and using this as the basis, he suggested three general formulae, (II) and (III) being representative of Tilden's classes (i) and (ii), whilst (IV) represented the sesquiterpenes.[§]



(I)

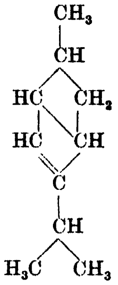
---

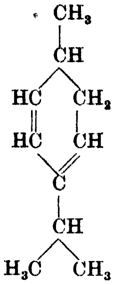
[*] *Ber.* 1873, **6**, 439.

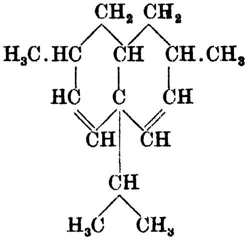
[†] *Ibid.* 1878, **11**, 152, 1698.

[‡] *Annalen*, 1887, **238**, 78.

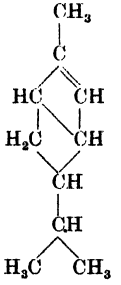
[§] It has been pointed out by Kondakov (*J. pr. Chem.* 1909 [ii], **80**, 455) that Wallach was anticipated in his suggestion that pinene contained a para bond by Kanonnikov, who made similar suggestions in a pamphlet entitled, *Über einige Eigenschaften der Terpene und ihr Verhalten zu einander*, published in Kasan in 1880. This pamphlet, which was written in the Russian language, was unfortunately overlooked by subsequent workers and exerted little influence on the development of terpene chemistry.

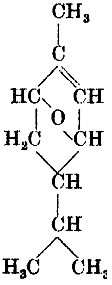

(II)

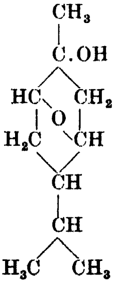

(III)


(IV)

Wallach considered that the reactions of pinene were in accord with a substance of formula (II) but some years later* he modified it somewhat to (V); pinol was regarded as the unsaturated oxide (VI) and sobrerol as (VII), both being formed by the fission of the para bond. The evidence leading to these formulae has been discussed already (Vol. I, p. 437).


(V)


(VI)


(VII)

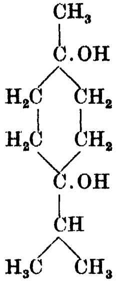
This formula for pinene accounted for its hydration to terpin (VIII), which would pass readily into cineole (IX) and terpineol (X).† An explanation was also afforded for the isomerisation of pinene to the monocyclic hydrocarbons, dipentene, terpinene and terpinolene, together with the oxidation of pinol to terpenylic and terebic acids.

In reviewing the evidence which was available at the time, there seems to be adequate justification for the view expressed

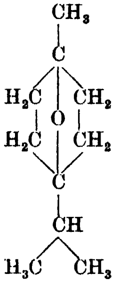
---

* *Ber.* 1891, **24**, 1552; *Annalen*, 1892, **268**, 210.

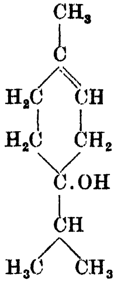
† At the time of these experiments, revision of these incorrect formulae for terpin, cineole, and terpineol had not been made.



(VIII)



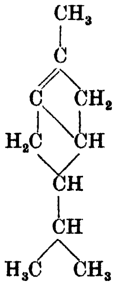
(IX)



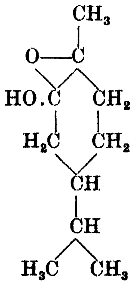
(X)

by Wallach, that the constitution of pinene was firmly established, and the formula advocated received support from the observation of Brühl,[*] who deduced from a determination of its molecular refraction that the hydrocarbon contained only one ethylenic linkage.

The modified formulae for pinene and sobrerol (XI) and (XII) suggested by Wagner[†] in 1891 do not, as remarked by Wallach,[‡] show any real advance, but they are of importance, since they led Wagner to devise experiments which later resulted in a solution of the problem of the constitution of pinene.



(XI)



(XII)

As mentioned previously (Vol. I, p. 437), pinol was first obtained by Wallach and Otto[§] as a by-product in the preparation of pinene nitrosochloride. On treatment with bromine it yields a dibromide from which, by the action of lead hydroxide, pinol glycol can be prepared.[*] These reactions may be represented schematically:

---

[*] *Annalen*, 1886, **235**, 66.

[†] *Ber.* 1891, **24**, 218.

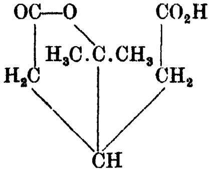
[‡] *Annalen*, 1892, **268**, 210.

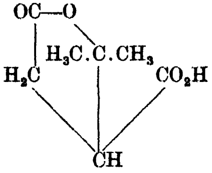
[§] *Ibid.* 1889, **253**, 249.

$$C_{10}H_{16} \longrightarrow C_{10}H_{16}O \longrightarrow C_{10}H_{16}OBr_2 \longrightarrow C_{10}H_{16}O(OH)_2.$$

Both Wagner and Wallach regarded pinol as an oxidation product of pinene, whilst Wagner considered pinol glycol to be a direct oxidation product of pinol. This being the case, the glycol must be formed by the oxidation of an ethylenic linkage, —CH:CH— → —CHOH—CHOH—, since this reaction had been observed by Wagner to be general. He now drew attention to the somewhat remarkable fact that, whereas both pinene and pinol gave on oxidation *terebic acid* (XIV), pinol glycol gave *terpenylic acid* (XIII).

It was known at the time from the synthetical investigations of Schryver[†] that Wallach's suggestion[‡] that terpenylic acid was the lactone of β-*iso*propylideneglutaric acid was correct, and that terebic acid was obviously the lower homologue. Wagner[§] now showed that if pinol was carefully oxidised with potassium permanganate it did actually give pinol glycol, a direct proof of the presence of an ethylenic linkage in pinol, and that on further oxidation terpenylic acid was obtained. Since the arrangement of eight of the ten carbon atoms in pinol glycol is thus established, it only remained to determine the position of the group $-\overset{|}{\underset{|}{C}}.CH_3$. If the oxidation of pinol to pinol glycol and terpenylic acid proceeds without any molecular rearrangement, then obviously pinol can only have either formula (XV) or (XVI) and the glycol (XVII) or (XVIII). An inspection of these formulae shows that the degradation of either (XVII) or (XVIII)


(XIII)


(XIV)

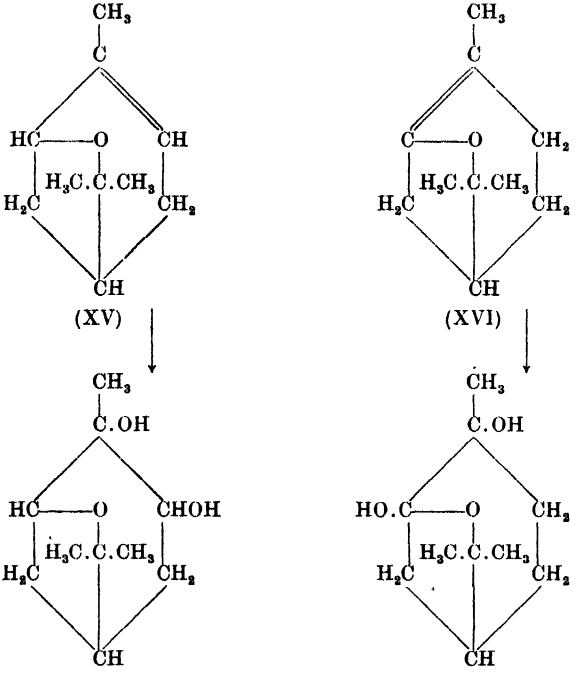
---

[*] Wallach, *Annalen*, 1890, **259**, 311; 1892, **268**, 222.

[†] *J.C.S.* 1893, **63**, 1327.

[‡] *Annalen*, 1890, **259**, 322.

[§] *Ber.* 1894, **27**, 1644.


(XV) (XVI)

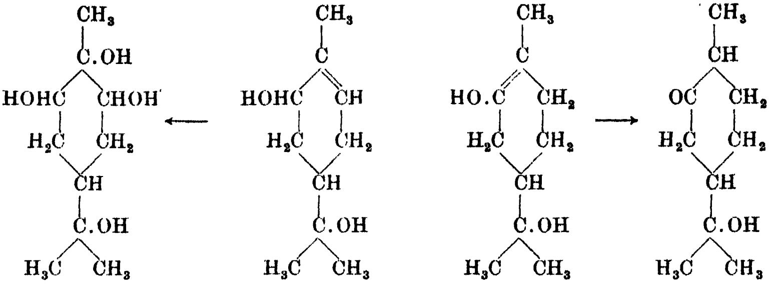
(XVII) (XVIII)

would lead to terpenylic acid. These constitutional formulae for pinol and pinol glycol are supported by the experiments of Wagner and Ginzberg* on the oxidation of pinol hydrate or, as it is usually called, sobrerol. Sobrerol was considered by Wallach to be the saturated oxide-alcohol (VII) (p. 108), whilst Wagner now regarded it as an unsaturated glycol, which might have either formula (XIX) or (XX), depending upon whether pinol was (XV) or (XVI). In the former case an *erythritol* (XXII) should result on careful oxidation, the formula (XX) being considered improbable, since a substance possessing this constitution might be expected to show the properties of the tautomeric *ketonic alcohol* (XXI).

Wagner and Ginzberg found that, on oxidation, sobrerol actually gave an erythritol, and it now became possible to account for the difference in properties between pinol and sobrerol, and

---

* *Ber.* 1894, 27, 1644; 1896, 29, 1195.



(XXII) (XIX) (XX) (XXI)

also to suggest a new formula for pinene (XXIII) which explained readily not only the formation of these substances but also its hydration to α-terpineol (XXIV) and the dehydration of this alcohol to dipentene (XXV). The various reactions which are involved are shown in the scheme on p. 113.

Whilst these reactions were all very simply accounted for by Wagner's formula for pinene, there was no direct evidence of the presence of the *cyclo*butane ring and, in view of its novelty, it is not remarkable that it did not at first meet with general approval. It was only firmly established after a series of remarkable investigations, which we owe to the genius of Baeyer,* and to a somewhat lesser extent to those of Tiemann and Semmler.† Before, however, proceeding to a consideration of these, it will be convenient to describe here some other experiments of Wagner, which led him to suggest an alternative formula for pinene.

By the oxidation of pinene with cold dilute potassium permanganate solution (1 per cent.) Wagner‡ obtained a glycol,§ $C_{10}H_{16}(OH)_2$, which, when treated with dilute sulphuric acid, gave pinol. The conversion into pinol proceeded evidently by the hydration of the *cyclo*butane ring in the glycol with the formation of the menthane-triol (XXVI), which by loss of water passed into sobrerol and finally into pinol. The facility with which the glycol passed into pinol led Wagner to suggest the possibility that pinene might be represented by (XXIIIa), the reactions then

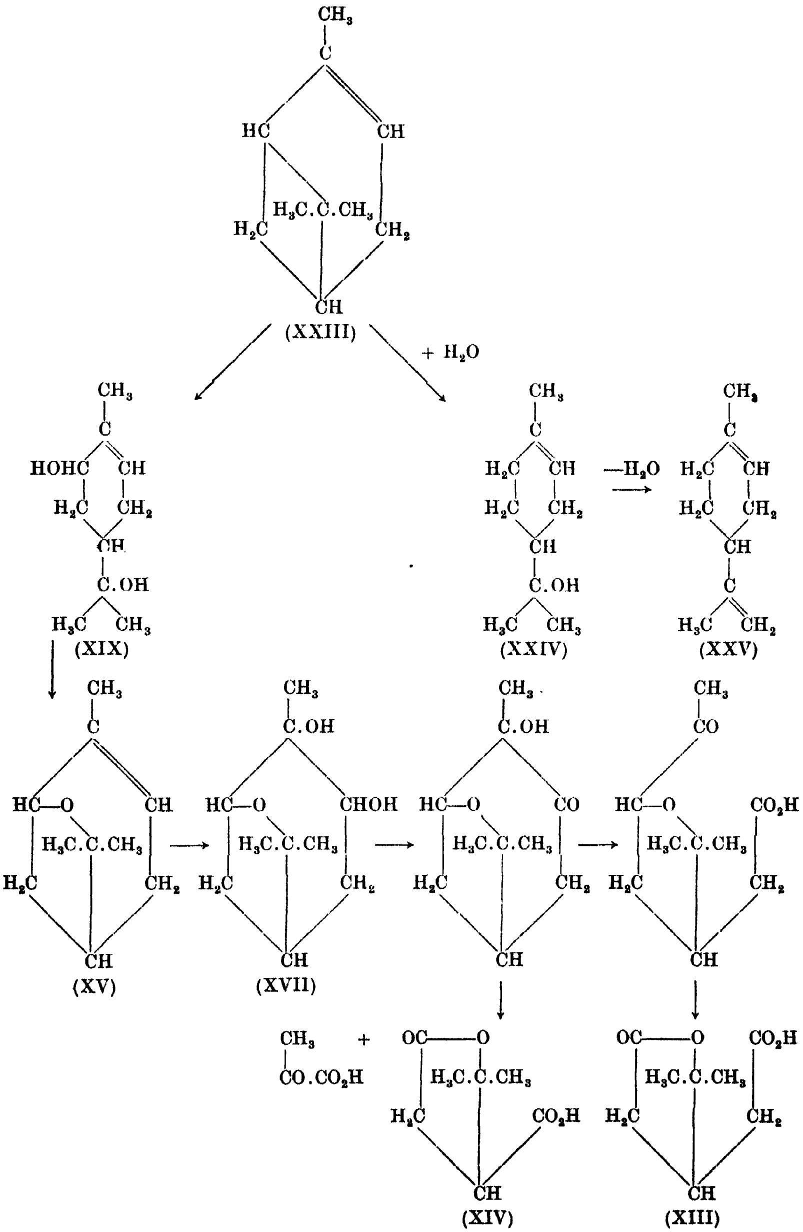
---

* *Ber.* 1896, **29**, 3, 326, 1907, 2775.

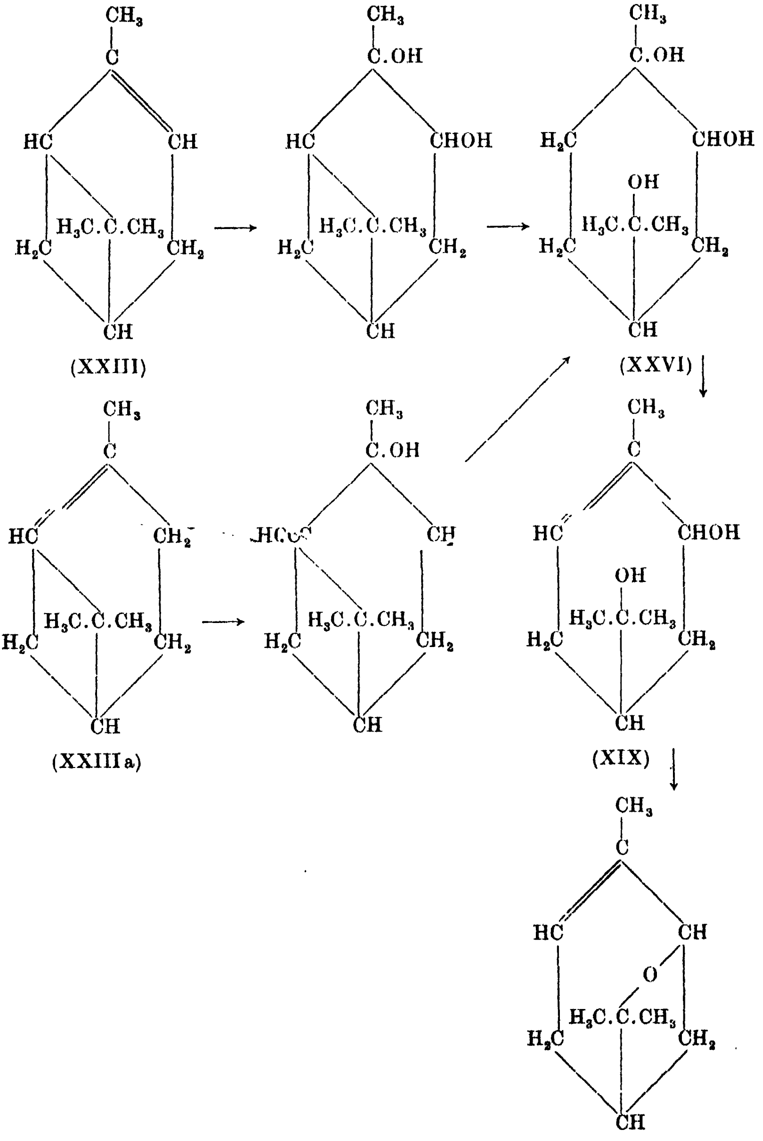
† *Ibid.* 1895, **28**, 1344; 1896, **29**, 128, 529.

‡ *Ibid.* 1894, **27**, 2270.

§ Subsequent experiments (p. 145) have shown this glycol to be actually a derivative of β-pinene, the existence of which was at the time unknown. This fact does not affect Wagner's argument.


(XXIII)
+ H₂O
(XIX)
(XXIV)
—H₂O
(XXV)
(XV)
(XVII)
CH₃ + CO.CO₂H
(XIV)
(XIII)

proceeding in accordance with one of the two schemes set out below.



(XXIII)

(XXVI)

(XXIIIa)

(XIX)

(XV)

The classical experiments of Baeyer, which must now be discussed, showed beyond question that pinene could only be represented by (XXIII). At the time (1895) when Baeyer carried out these experiments, he had established the presence of a *cyclo*propane ring in the dicyclic ketone, *carone* (p. 77), and it is not surprising, therefore, that the formula suggested by Wagner made a special appeal to him, the more especially so, since the early work on the synthesis of polymethylene derivatives had been carried out by Perkin in his laboratory.[*] Baeyer studied the acids which were formed by the oxidation[†] of pinene with potassium permanganate, which he showed to consist mainly of (*a*) a ketonic monobasic acid, *pinonic acid*, $C_{10}H_{16}O_3$, and (*b*) a ketonic dibasic acid, *pinoylformic acid*, $C_{10}H_{14}O_5$. Pinonic acid was found to contain a $CH_3.CO$— group, since, on treatment with sodium hypobromite, it passed quantitatively into bromoform and a dibasic acid, *pinic acid*, $C_9H_{14}O_4$. The formation of an acid containing the group $CH_3.CO$— could only be explained, in the absence of isomerisation, by the acceptance of formula (XXIII) for pinene, when pinonic acid would be (XXVII) and pinic acid (XXVIII).

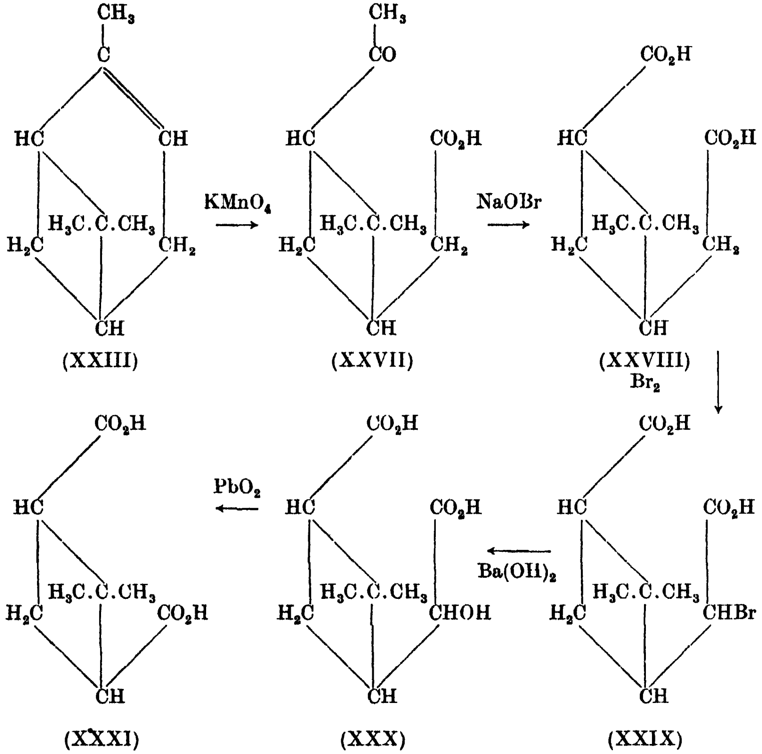
Direct evidence of the presence of the *cyclo*butane ring structure in pinonic and pinic acids was not readily obtained. Although, as will be seen from the experiments to be discussed, pinonic acid is unstable, pinic acid is remarkably stable and is obviously a cyclic acid. From the latter, by the action of bromine, *bromopinic acid* (XXIX) was prepared, which on digestion with barium hydroxide gave *hydroxypinic acid* (XXX). This acid was an α-hydroxy acid, since it gave on oxidation with lead peroxide a dibasic acid, *norpinic acid* (XXXI), which, like pinic acid, showed remarkable stability and resisted all further attempts at degradation. Although it was not until many years later that synthetic proof of the correctness of Baeyer's formula for norpinic acid was obtained (see p. 154), indirect evidence was supplied by a study of the properties of pinonic acid and pinoylformic acid.

Baeyer found that when pinonic acid was treated with dilute mineral acids, ring fission occurred with formation of a ketonic lactone, ***homoterpenyl methyl ketone*** (XXXIII), a substance which

---

[*] Compare Perkin, Pedler Lecture, *J.C.S.* 1929, p. 1347.

[†] A detailed discussion of this oxidation is deferred to p. 145.



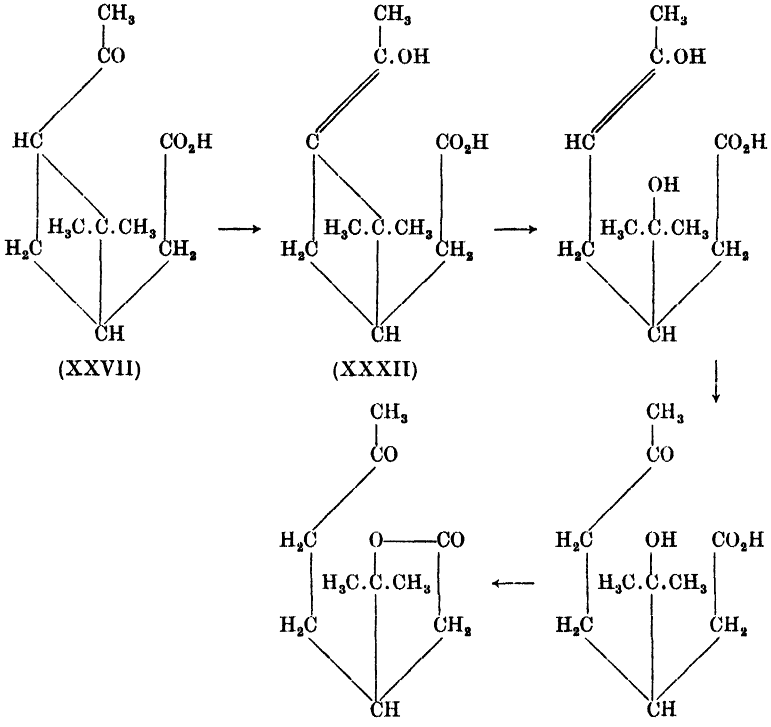
had already been prepared by Wallach* from α-terpineol (cf. Vol. I, p. 259). The instability of the *cyclo*butane ring in pinonic acid is evidently due to the tendency of the carbonyl group to enolise (XXXII), the conversion into the ketonic lactone then proceeding in accordance with the scheme shown.

Pinoylformic acid resembled in its general properties pinonic acid and Baeyer represented it by (XXXIV) (p. 118). It was characterised as a ketonic dibasic acid by the preparation of the *phenylhydrazone*, m.p. 192·5°, and was undoubtedly the α-ketonic dibasic acid corresponding to pinonic acid, since, on oxidation with lead peroxide, it passed into pinic acid (XXVIII).

Like pinonic acid, and for the same reason, pinoylformic acid was readily converted into a lactone by ring fission, giving on

---

* *Ber.* 1895, **28**, 1775; *Annalen*, 1893, **275**, 153.



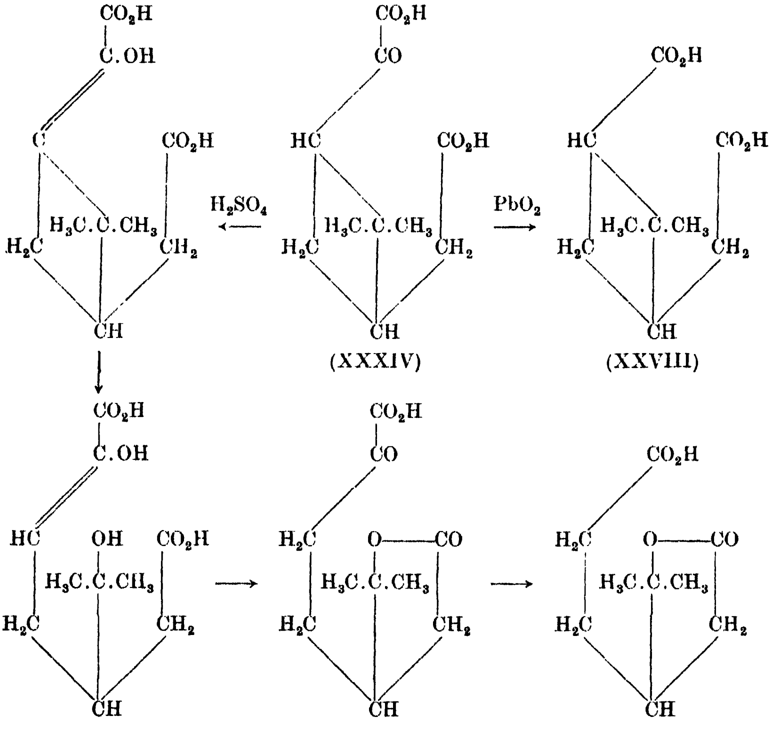
(XXVII) (XXXII) (XXXIII)

treatment with dilute sulphuric acid *homoterpenylformic acid* (XXXV). The constitution of this acid was proved by its ready oxidation to *homoterpenylic acid* (XXXVI), m.p. 100–101°, synthesised many years later by Simonsen,* together with terpenylic and terebic acids.

During these experiments Baeyer separated from amongst the oxidation products of pinene a small quantity of an acid, which gave a sparingly soluble sodium salt. This acid, *nopinic acid*, was isomeric with pinonic acid, but was an α-hydroxy acid, since it gave on oxidation with lead peroxide a ketone, *nopinone*, $C_9H_{14}O$. Baeyer recognised that this acid could not be derived from the same hydrocarbon as pinonic acid and it was obvious that pinene was not homogeneous, but a mixture of two hydrocarbons,

---

* *J.C.S.* 1907, **91**, 190.



(XXXIV) (XXVIII)

(XXXV) (XXXVI)

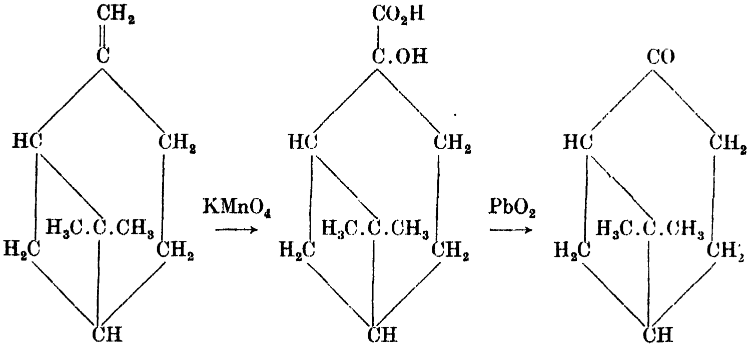
(i) *α-pinene*, which had the Wagner formula (XXIII) and gave on oxidation pinonic acid, and (ii) *β-pinene* giving on oxidation nopinic acid. This latter hydrocarbon was in all probability (XXXVII), having an exocyclic ethylenic linkage, when nopinic acid would be (XXXVIII) and nopinone (XXXIX). Subsequent experiments, which were carried out with α-pinene prepared from the nitrosochloride, confirmed this conclusion, since the hydrocarbon did not yield any nopinic acid.*

Although Baeyer had apparently provided a rigid experimental proof of the correctness of Wagner's formula for α-pinene, some doubt appeared to be cast upon it by the contemporaneous experiments of Tiemann and Semmler.† In contradiction to

---

* Baeyer suggested later an erroneous explanation to account for the formation of nopinic acid from α-pinene (cf. p. 192).

† The more important references to this work are given on p. 112.



(XXXVII) (XXXVIII) (XXXIX)

Baeyer, these authors found that the ketonic acid, $C_{10}H_{16}O_3$, which was formed by the oxidation of pinene,* was an oil which did not yield a dibasic acid and bromoform when treated with sodium hypobromite.

This liquid acid they called pinonic acid and they suggested that Baeyer's acid was an isomeric acid, which they designated α-pinonic acid. To obtain an insight into the constitution of pinonic acid Tiemann and Semmler investigated the products formed when it was oxidised with nitric acid, chromic acid and potassium permanganate in hot alkaline solution. With nitric acid only terebic acid was obtained, whilst with chromic acid a number of important degradation products were formed, the chief being (i) a ketonic dibasic acid, iso*ketocamphoric acid*, $C_{10}H_{16}O_5$, identical with an acid prepared previously by Thiel† by the oxidation of *α-campholenic acid*, (ii) a tribasic acid, iso*camphoronic acid*, $C_9H_{14}O_6$, and (iii) terebic acid. From the oxidation with potassium permanganate they obtained (i) a tribasic acid, *dimethyltricarballylic acid*, $C_8H_{12}O_6$, (ii) a hydroxy dibasic acid, *hydroxydimethylsuccinic acid*, $C_6H_{10}O_5$, and (iii) a lactonic dibasic acid, $C_9H_{12}O_6$, the *lactone* of *hydroxy*iso*camphoronic acid*, $C_9H_{14}O_7$.

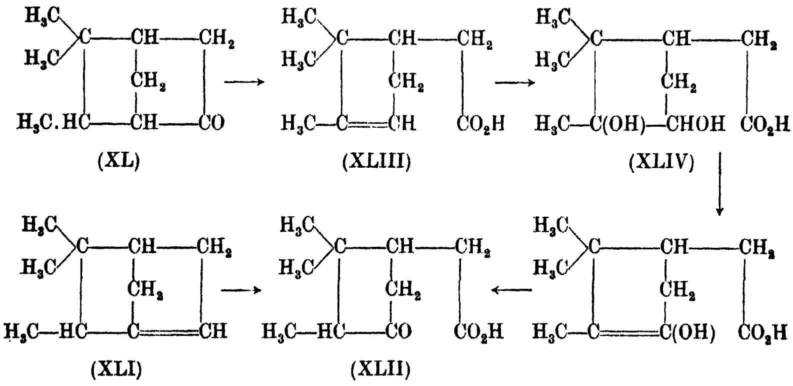
These degradation products were considered by Tiemann and Semmler to indicate a very close structural relationship between pinene and camphor, a view which was supported by the claim‡ that *α-campholenic acid* could be converted through dihydroxy-dihydro-α-campholenic acid into pinonic acid. It had been suggested by Tiemann[*] that camphor was most probably represented by formula (XL), and he therefore advanced formula (XLI) for pinene, when pinonic acid would be the *cyclo*pentane acid (XLII). This formula would account also for its formation from α-campholenic acid (XLIII), since this acid yields on oxidation the dihydroxy acid (XLIV), which would on distillation pass into pinonic acid (XLII). It is only recently that it has been shown[†] that the substance obtained by Tiemann was not pinonic acid, but *α-campholonic acid*, which does, in fact, have the structure (XLII).

---

* In all the experiments carried out during this period the pinene used was a mixture of α- and β-pinenes of varying degrees of optical purity.

† *Ber.* 1893, **26**, 922.

‡ Tiemann, *Ber.* 1896, **29**, 3014.



To account for the existence of Baeyer's crystalline pinonic acid for which they accepted the *cyclo*butane structure, Tiemann and Semmler[‡] suggested that it was formed in accordance with the scheme set out on p. 121, when the hypothetical oxide (XLV) might pass either into a *cyclo*pentane or *cyclo*butane ring.

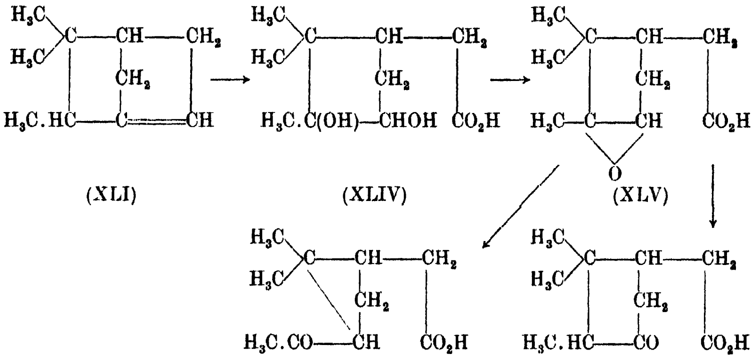
Shortly afterwards Tiemann and Semmler found that their liquid pinonic acid could be obtained crystalline and appeared to be identical with Baeyer's acid. They concluded therefore that the *cyclo*butane acids, pinic and norpinic acids, were formed from pinonic acid by a molecular rearrangement.

---

[*] *Ber.* 1895, **28**, 1079.

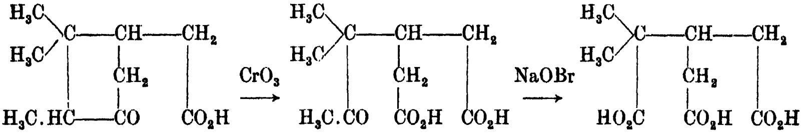
[†] Komppa and Beckmann, *Ber.* 1936, **69**, 2783; Delépine, *Bull. Soc. chim.* 1937 [v], **4**, 1145.

[‡] *Ber.* 1896, **29**, 128.



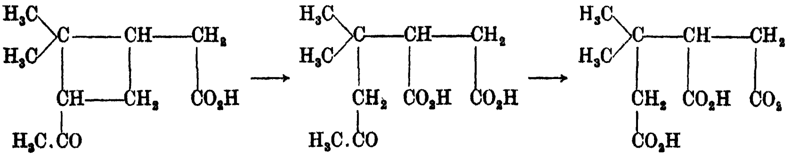
(XLI) (XLIV) (XLV) (XXVII) (XLII)

It is necessary now to consider in greater detail the evidence, outlined above, upon which their *cyclo*pentane formula for pinonic acid was based. The oxidation with chromic acid to *iso*ketocamphoric acid (XLVI) and *iso*camphoronic acid (XLVII) was considered to proceed in the following manner:



(XLII) (XLVI) (XLVII)

Since *iso*ketocamphoric acid, m.p. 129–130·5°, *semicarbazone*, m.p. 187°, *oxime*, m.p. 185–186°, was oxidised by sodium hypobromite to *iso*camphoronic acid,* it was of fundamental importance to determine the constitution of the latter acid, more especially since Baeyer formulated the reactions mentioned above in the following manner, *iso*ketocamphoric acid and *iso*camphoronic acid being given the alternative formulae (XLVIII) and (XLIX) respectively:



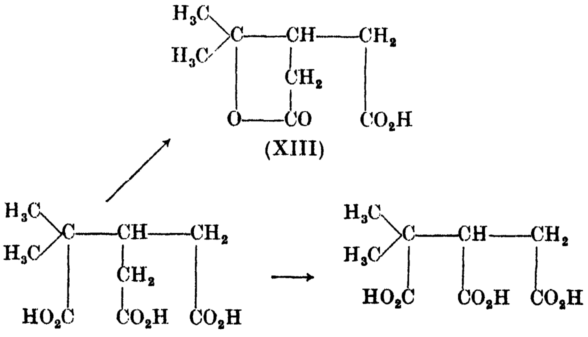
(XXVII) (XLVIII) (XLIX)

---

* Tiemann and Semmler, *Ber.* 1895, **28**, 1348.

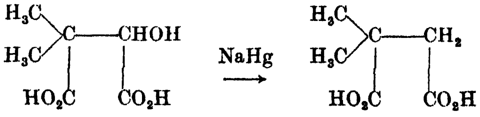
If Baeyer's formula for *iso*camphoronic acid was correct, it was difficult to explain the observation of Tiemann and Semmler that this acid, when treated with concentrated sulphuric acid, gave terpenylic acid and, on further oxidation with potassium permanganate, dimethyltricarballylic acid (L), two substances which are readily derivable from an acid having the formula (XLVII).

The synthesis of *iso*camphoronic acid by Perkin* furnished conclusive proof that this acid had the formula which had been given to it by Tiemann and Semmler. It may be mentioned that Perkin and Thorpe† had previously prepared an acid having the constitution suggested by Baeyer, which had, however, properties completely different from those of *iso*camphoronic acid. It follows therefore that Tiemann and Semmler's formula (XLVI) for *iso*ketocamphoric acid must also be correct.


(XIII)

(XLVII)

(L)


(LI)

(LII)

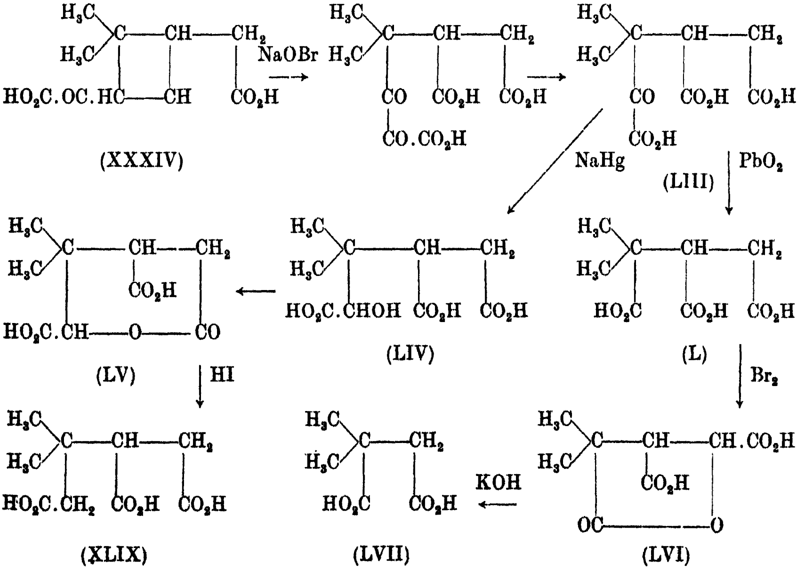
Attention must be given to the products obtained from pinonic acid on oxidation with potassium permanganate (p. 119). Two of these afford little difficulty: the *dimethyltricarballylic acid*, m.p. 149–151°, *anhydride*, m.p. 145–146°, must be (L), since it is identical with the acid obtained by the oxidation of *iso*camphoronic acid, whilst the *hydroxydimethylsuccinic acid* must have formula (LI), since on reduction it yields as-*dimethylsuccinic acid* (LII). Before, however, proceeding to a consideration of the other acid which was obtained, namely the *lactone* of *hydroxy*iso*camphoronic acid*, m.p. 143·5°, it is necessary to refer to some experiments of Baeyer on the degradation of pinoylformic acid, which resulted in the preparation of an isomeric *lactone*, m.p. 186°.

---

* *J.C.S.* 1902, 81, 246.

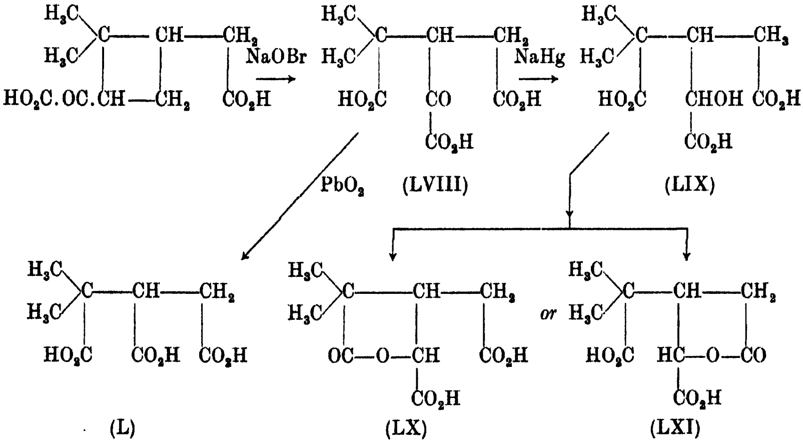
† *Ibid.* 1899, 75, 897.

When pinoylformic acid (XXXIV) is oxidised with sodium hypobromite, it gives a ketonic tribasic acid, *α-keto*iso*camphoronic acid*, $C_9H_{12}O_7$, m.p. 186–187°, the reaction being formulated by Baeyer in accordance with the scheme given below, fission of the *cyclo*butane ring being assumed to occur with the intermediate formation of a diketonic acid. Oxidation of α-keto*iso*camphoronic acid with lead peroxide gave dimethyltricarballylic acid (L) identical with the acid obtained by Tiemann and Semmler by the oxidation of pinonic acid with chromic acid. The constitution of the tricarballylic acid was proved by Baeyer, who showed that on bromination it gave the *lactone* of *hydroxydimethyltricarballylic acid* (LVI), which, on fusion with potassium hydroxide, yielded as-*dimethylsuccinic acid* (LVII) and oxalic acid.



The reduction of α-keto*iso*camphoronic acid (LIII) with sodium amalgam led to a *hydroxy* acid (LIV), which was isolated in the form of a *lactone*, m.p. 186°, which Baeyer represented by (LV), since, on reduction with hydriodic acid, *iso*camphoronic acid (XLIX) was obtained. Now it has been proved by the synthetical experiments of Perkin that *iso*camphoronic acid cannot have the formula (XLIX), and it follows therefore that, unless a profound molecular rearrangement occurs on reduction of the lactone, it cannot have formula (LV).

It was pointed out by Perkin and Thorpe* that α-keto*iso*camphoronic acid must have formula (LVIII), the reaction investigated by Baeyer actually proceeding in accordance with the scheme:



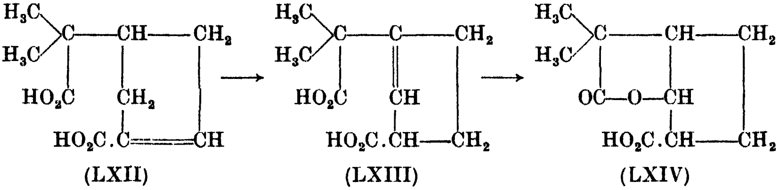
(LVIII) (LIX)

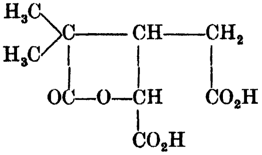
(L) (LX) (LXI)

If this scheme be correct, and if the proof of the constitution of the lactonic acid discussed be regarded as established, the conversion of pinoylformic acid into α-keto*iso*camphoronic acid involves a molecular rearrangement. A consideration of the formula of the *hydroxy* acid (LIX) formed by the reduction of α-keto*iso*camphoronic acid shows that the hydroxy group is in the γ-position to two of the carboxyl groups and it can therefore give rise to two lactones (LX) and (LXI); further, both these lactones can exist in *cis-trans*-modifications. Confirmation of Perkin and Thorpe's formula for Baeyer's lactone has been obtained from quite a different field of research. It was found by Aschan[*] that *dehydrocamphenic acid* (LXII) on oxidation with dilute nitric acid gave a lactonic acid, $C_9H_{12}O_6$, m.p. 256°. This lactone, when heated to 100° with sulphuric acid, isomerised to a lactonic acid, m.p. 185–186°, undoubtedly identical with Baeyer's lactonic acid. The two acids, m.p. 256° and 185–186°, were regarded by Aschan as *cis-trans*-isomerides, the higher melting and less soluble acid being, according to convention, assigned the *trans*-configuration.[†] According to Lipp[‡] the oxidation of dehydrocamphenic acid (LXII) proceeds in the following manner. On warming the unsaturated acid with dilute nitric acid it passes first into the isomeride (LXIII),[§] which being a $\beta:\gamma$-unsaturated acid gives the *lactone* (LXIV), which is then oxidised to the lactonic acid, m.p. 256° (LX).

---

* *J.C.S.* 1913, **103**, 1761.




(LX)

Aschan showed that both lactonic acids (m.p. 256° and 185–186°) gave on reduction *iso*camphoronic acid, whilst on fusion with potassium hydroxide, formic, succinic and *iso*butyric acids were obtained. This latter reaction Lipp regarded as a satisfactory proof of the constitution of the lactonic acids, fission occurring as indicated by the dotted lines.

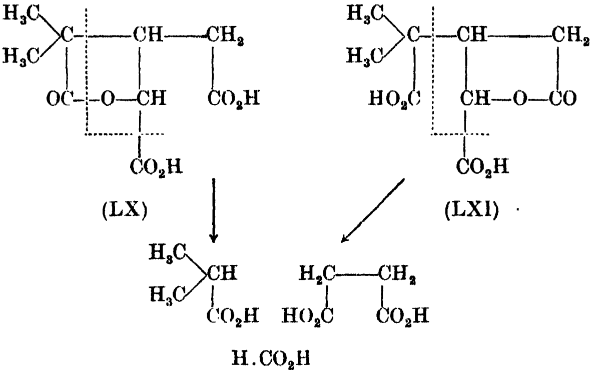
---

[*] *Annalen*, 1910, **375**, 336; 1913, **398**, 303.

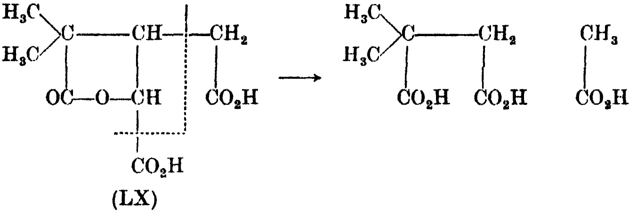
[†] Since Aschan retained Baeyer's formula for *iso*camphoronic acid, which the synthetical investigations of Perkin have shown to be erroneous, the formulae suggested by him for the lactonic acids need not be considered.

[‡] *Ber.* 1914, **47**, 871.

[§] This is analogous to the change of α-campholenic acid into β-campholenic acid (see p. 439).

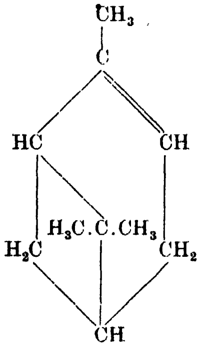


It has, however, been pointed out by Perkin and Thorpe that, if the decomposition proceeds in a manner analogous to that of the lactone derived from hydroxydimethyltricarballylic acid (p. 124), these three acids should actually be formed from a lactonic acid having the structure (LXI), whilst that having formula (LX) might be expected to give either dimethyl or trimethylsuccinic acid.

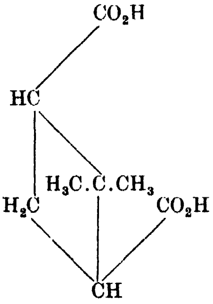


Although the constitution of Baeyer's lactonic acid cannot be regarded as rigidly proved, it is undoubtedly represented by either formula (LX) or (LXI), the latter, on the evidence at present available, being the more probable. If this conclusion be accepted, it follows, with a considerable degree of probability, that the isomeric lactonic acid, m.p. 143·5°, obtained by Tiemann and Semmler by the oxidation of pinonic acid with potassium permanganate (p. 119), must be either the *cis*- or *trans*-modification of (LX).

The main analytical evidence bearing on the constitution of α-pinene has now been outlined, and it remains only to discuss in how far it supports Wagner's formula (XXIII) for this hydrocarbon. Whilst this formula is in complete accord with its hydration products, terpin and α-terpineol, and with its oxidation products, pinol and sobrerol, the main proof lies in the experimental investigations of Baeyer, and this proof would appear to be absolutely rigorous. There can be no doubt that norpinic acid is the *cyclo*butane acid (XXXI), since this has been established synthetically (p. 154). None of the reactions involved in the preparation of this acid is likely to cause any molecular rearrangement, and it seems justifiable to accept the presence of the *cyclo*butane ring in α-pinene (XXIII).



(XXIII)

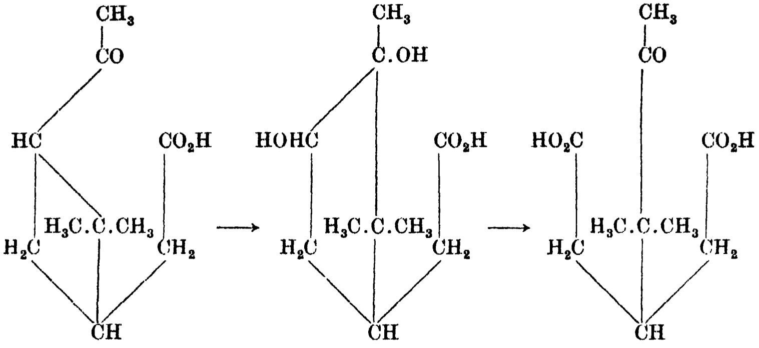


(XXXI)

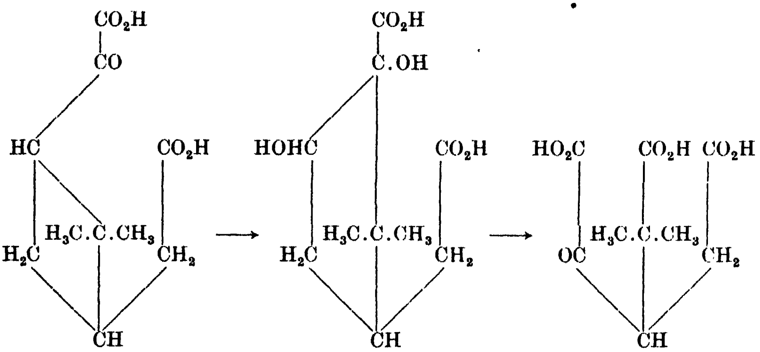
There are two[*] abnormal reactions to which reference has already been made, which may now be summarised. Firstly, there is the oxidation of pinonic acid to *iso*ketocamphoric acid (XLVI). This change must be assumed to take place by a pinacolic rearrangement to give, as intermediate, the dihydroxy compound (LXV), which then undergoes a normal oxidation. Secondly, the conversion of pinoylformic acid (XXXIV) into α-keto*iso*camphoronic acid (LVIII) by the action of sodium hypochlorite probably proceeds in an analogous manner, the oxidation being in this case, however, more profound. The theory of these rearrangements is discussed later (p. 159).

---

[*] It has already been pointed out (p. 120) that the alleged formation of pinonic acid from α-campholenic acid is erroneous and that the oxidation of the latter acid is not abnormal.



(XXVII) (LXV) (XLVI)

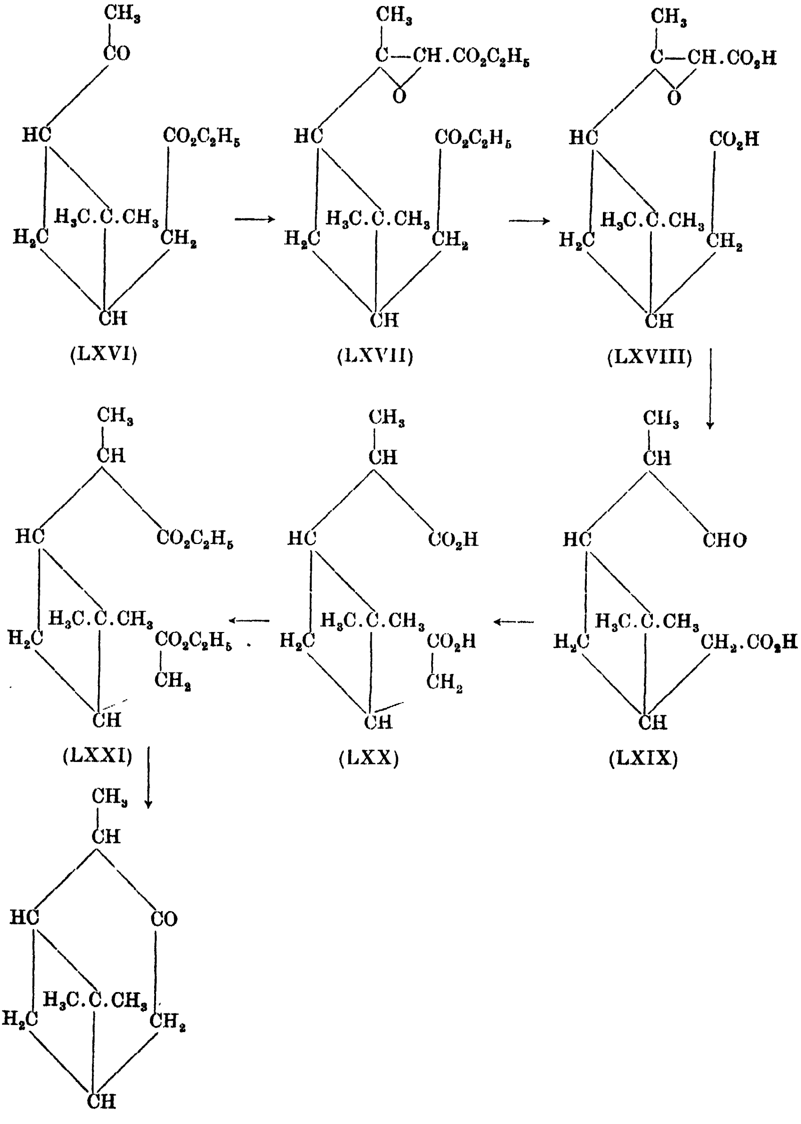


(XXXIV) (LVIII)

It may be concluded that Wagner's formula for α-pinene is established on a firm analytical basis; confirmation by synthesis has long been sought, but it is only recently that complete success has been achieved. An ingenious partial synthesis was carried out by Ruzicka and Trebler.* The starting-point was ethyl *dl*-pinonate (LXVI) which, when condensed with ethyl chloroacetate in the presence of sodium ethoxide, gave the *glycidic ester* (LXVII), b.p. 140–150°/0·1 mm., and from this, by hydrolysis, the *acid* (LXVIII), m.p. 128°, was prepared. When this acid was heated above its melting-point it gave *homopinocamphoraldehyde* (LXIX), b.p. 130–140°/0·3 mm., *semicarbazone*, m.p. 193–195°, and this aldehyde, on oxidation with potassium permanganate, was converted into *homopinocamphoric acid* (LXX), an oil, the *ethyl* ester (LXXI) of which boiled at 130°/1 mm.

---

* *Helv. Chim. Acta*, 1920, **3**, 756; 1921, **4**, 666; 1924, **7**, 489.



(LXVI) (LXVII) (LXVIII)

(LXXI) (LXX) (LXIX)

(LXXII)

An attempt to convert homopinocamphoric acid into the dicyclic ketone by distillation of the lead salt was unsuccessful,* but, by the action of sodium on the ethyl ester in xylene solution, a ketonic ester was obtained, which on hydrolysis with dilute hydrochloric acid gave dl-*pinocamphone*† (LXXII) identical in all respects with the ketone which had been previously prepared (see p. 226).

The next stage in the synthesis involved a reduction of *pinocamphoneoxime* (LXXIII) to *pinocamphylamine* (LXXIV), a base described previously by Wallach‡ and by Tilden§ (see p. 232). This base was converted by the usual methods into *pinocamphyltrimethylammonium hydroxide* (LXXV), which, on distillation under diminished pressure, gave a mixture of a hydrocarbon and *pinocamphyldimethylamine* (LXXVI). The hydrocarbon so prepared was not pure α-pinene, but was a mixture of α-pinene (XXIII) and δ-pinene (LXXVII), a result which was to be anticipated from the method of preparation. α-Pinene was readily identified in the mixture by the preparation of pinene nitrosochloride, whilst, on oxidation, in addition to pinonic acid, *pinocamphoric acid* (LXXVIII), m.p. 186–187°, an acid originally prepared by Wallach‖ by the oxidation of pinocamphone, was obtained. Since both pinocamphone and pinonic acid have subsequently been synthesised (see pp. 148, 228), this amounts to a total synthesis of α-pinene.

A partial synthesis of α-pinene had been described many years before by Tschugaev,¶ who prepared the hydrocarbon by the distillation of *methyl* l-*pinocamphylxanthate* (LXXIX). In this case also, the hydrocarbon was undoubtedly a mixture of α- and δ-pinenes, since Gildemeister and Köhler** have shown that on oxidation an acid, one of the optically active modifications of pinocamphoric acid (LXXVIII), m.p. 192°, is obtained. Reference is made later (p. 198) to the formation of α-pinene by the isomerisation of β-pinene; it is also probably formed by the reduction of verbenene (see p. 220).

---

[*] Compare Bonsdorff, *Ber.* 1911, **44**, 3208.

[†] From ethyl *l*-pinonate Ruzicka and Trebler prepared a small quantity of *l*-pinocamphone, but this was not obtained pure.

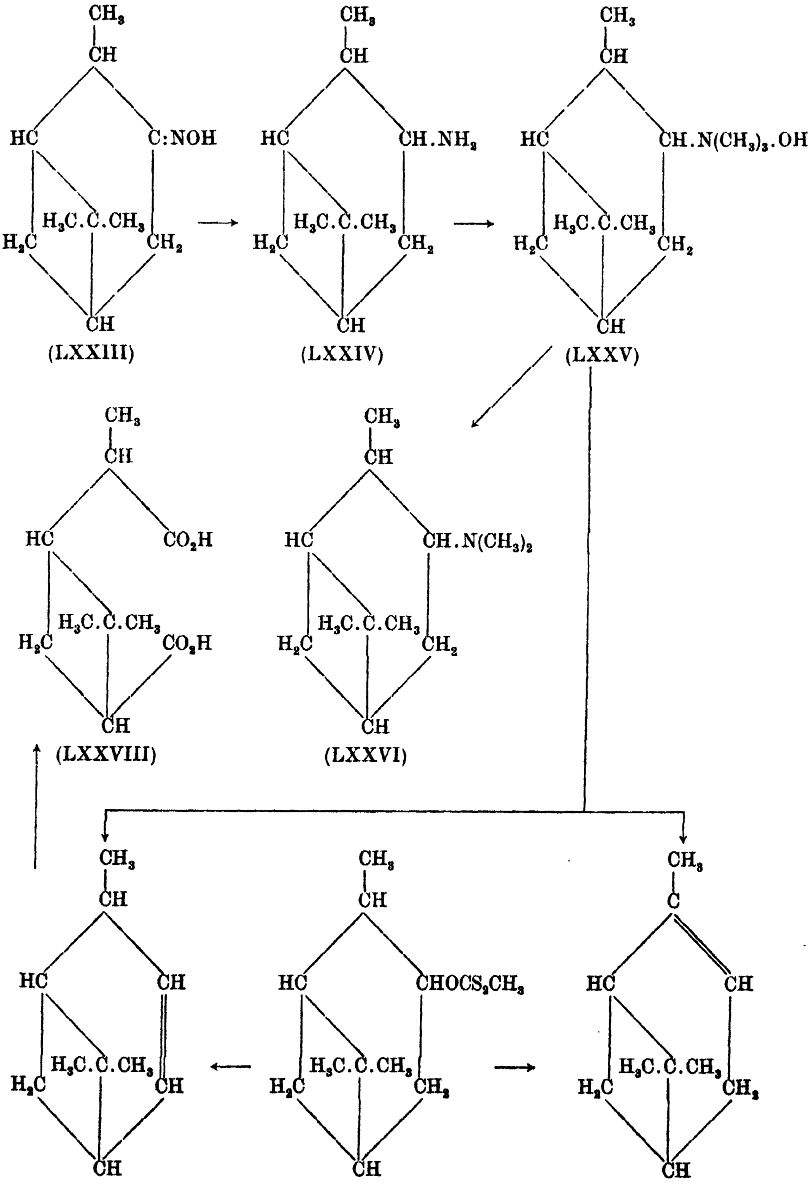
[‡] *Annalen*, 1900, **313**, 367.

[§] *J.C.S.* 1906, **89**, 1560.

[‖] *Annalen*, 1906, **346**, 236.

[¶] *J. Russ. Phys. Chem. Soc.* 1907, **39**, 1324.

[**] *Wallach Festschrift*, 1909, p. 414. Compare p. 209.



(LXXIII) (LXXIV) (LXXV)

(LXXVIII) (LXXVI)

(LXXVII) (LXXIX) (XXIII)

α-Pinene can be characterised by the preparation of the *nitrosochloride*, which usually melts at 103°, although higher melting-points have been recorded (see p. 179). The identity may be confirmed by conversion of the nitrosochloride into the *nitrolpiperidide*, m.p. 118–119°, or the *nitrolbenzylamine*, m.p. 122–123°. If the α-pinene has a high optical rotatory power, the crystalline optically inactive nitrosochloride may fail to separate, for reasons which are discussed on p. 179. In such cases the presence of the hydrocarbon can be established by its oxidation with potassium permanganate to pinonic acid.

Since α-pinene contains two asymmetric carbon atoms, the hydrocarbon, as separated from the various essential oils, shows marked variations in its optical power and the preparation of the optically pure terpene free from isomerides is a matter of considerable difficulty. The configuration of the α-pinene molecule is such that only one relatively unstrained structure is likely to exist, and it is therefore not surprising that no evidence of the existence of geometrical isomerides has been obtained.* Fuguitt, Stallcup and Hawkins,† by highly efficient fractional distillation, have obtained α-pinene free from the β-isomer, and give the following constants: b.p. 52·2°/20 mm., $d_{4°}^{25°}$ 0·8542, $n_D^{25°}$ 1·4631, $[\alpha]_D^{25°}$ $-3·83°$ (from gum turpentine), $[\alpha]_D^{25°}$ $+34·07°$ (from wood turpentine). According to Dupont and Desalbres‡ fractional crystallisation at a low temperature, −75°, has no advantage over fractional distillation as a method of purification, although the velocity of crystallisation serves as a good standard of purity. Darmois§ has found the pure *d*- and *l*-forms to melt at −50°, whilst they boil at 156°/760 mm., Dupont and Desalbres giving the following constants for the two forms: *d*-α-pinene, $d^{15°}$ 0·8620, $n_D^{12°}$ 1·4650, $[\alpha]_D$ $+48·85°$, velocity of crystallisation at −75°, 34 mm. per minute; *l*-α-pinene, $d^{15°}$ 0·8620, $n_D^{12°}$ 1·4649, $[\alpha]_D$ $-46·65°$, velocity of crystallisation at −75°, 16·3 mm. per minute. It is not improbable, although higher rotatory powers have been recorded, that these two specimens were nearly optically pure. This view is supported by the observations of

---

* The suggested presence of an isomeric form of *d*-α-pinene in Port Orford cedarwood oil (Thurber and Roll, *Ind. Eng. Chem.* 1927, **19**, 739) is unsupported by adequate experimental evidence.

† *J. Amer. C.S.* 1942, **64**, 2978.

‡ *Bull. Soc. chim.* 1923 [iv], **33**, 1252.

§ *Compt. rend.* 1909, **149**, 732.

Darmois,[*] who has shown that it is possible to estimate with a high degree of accuracy the percentage of *d*-α-pinene in admixture with *l*-α-pinene by a determination of the rotatory dispersion. *d*- and *l*-α-Pinenes of high purity have been prepared by Lynn[†] and by Thurber and Thielke[‡] by decomposition of the optically active nitrosochlorides (p. 180), the observed rotatory powers being $[\alpha]_D^{25^\circ} + 51{\cdot}14^\circ$ and $-51{\cdot}28^\circ$. Briggs and Taylor[§] have recorded a rotation of $[\alpha]_D^{25^\circ} + 53{\cdot}0^\circ$ for natural *d*-α-pinene.

dl-α-Pinene can be readily obtained in a state of purity and free from β-pinene by the decomposition of pinene nitrosochloride with aniline, a reaction discovered by Wallach[‖] (see p. 180), who observed the following values for the hydrocarbon purified in this manner: b.p. 155–156°, d^{20° 0·858, $n_D^{21^\circ}$ 1·4655. There is no evidence that *dl*-α-pinene is a racemic compound.[¶] The molecular refraction of α-pinene, 43·86, shows a slight exaltation over the calculated value, 43·54, but as has been pointed out by Östling,[**] the conjugation of an ethylenic linkage with the *cyclo*butane ring shows no special effect. The absorption spectrum of α-pinene in the ultra-violet has been found by Hantzsch to resemble that of limonene,[††] whilst the rotatory dispersion has been investigated by several workers.[‡‡] The Raman spectrum has been studied by Kastler[§§] and by Bonino and Cella.[‖‖] According to Roth and Östling[¶¶] the heat of combustion of α-pinene is 1480·7 kg.-cals.

The effect of high temperatures on α-pinene[***] under various conditions has been studied by a number of investigators. Berthelot[†††] found that when the hydrocarbon was heated under pressure at 250–270° dipentene was formed. By passing the vapour through a heated iron tube Tilden[*] obtained isoprene, *p*-cymene, benzene, toluene and *m*-xylene, whilst Schultz[†] working at a higher temperature obtained, in addition to the benzenoid hydrocarbons, naphthalene, anthracene, methylanthracene and phenanthrene. These early experiments have been confirmed by Sabatier, Maihle and Gaudion,[‡] who have found that aromatic hydrocarbons are obtained in varying yields, depending upon the temperature, when the terpene is vaporised over copper, nickel, cobalt and iron catalysts. Semmler and Jonas[§] have prepared a diterpene, b.p. 170–180°/10 mm., d^{20° 0·8892, n_D 1·5162, by heating α-pinene to 270°, whilst, when treated in admixture with isoprene by a concentrated solution of sulphuric acid in acetic acid, a sesquiterpene, b.p. 135–137°/16 mm., d^{20° 0·891, n_D 1·5014, is obtained.

---

[*] *Compt. rend.* 1909, **149**, 730; cf. Pariselle, *Ann. Chim.* 1923 [ix], **19**, 130.

[†] *J. Amer. C.S.* 1919, **41**, 361.

[‡] *Ibid.* 1931, **53**, 1030.

[§] *J. Org. Chem.* 1947, **12**, 551.

[‖] *Annalen*, 1890, **258**, 344.

[¶] Mitchell and Smith, *J.C.S.* 1913, **103**, 492.

[**] *J.C.S.* 1912, **101**, 457.

[††] *Ber.* 1912, **45**, 553.

[‡‡] Servant, *Compt. rend.* 1932, **194**, 368; Padmanabhan and Jatkar, *J. Amer. C.S.* 1935, **57**, 334; *J. Ind. C.S.* 1935, **12**, 518; Rule and Chambers, *J.C.S.* 1937, p. 151; compare Darmois, *loc. cit.*

[§§] *Compt. rend.* 1930, **191**, 565; compare Daure, *ibid.* 1934, **198**, 725.

[‖‖] *Nature*, 1930, **126**, 915; *Chem. Zentr.* 1937, I, 1917.

[¶¶] *Ber.* 1913, **46**, 323; compare Auwers, Roth and Eisenlohr, *Annalen*, 1910, **373**, 273; 1911, **385**, 107.

[***] In most of the early experiments carried out with pinene a mixture of α- and β-pinenes was used, but since β-pinene isomerises readily to α-pinene this factor is probably of little importance.

[†††] *Ann. Chim.* 1853 [iii], **37**, 223; **39**, 9; compare Wallach, *Annalen*, 1885, **227**, 282.

The isomerisation of α-pinene to dipentene occurs at comparatively low temperatures. It was suggested by Smith[‖] that α-pinene was slowly racemised when heated at 184° or 237° and that the reaction was monomolecular. This interpretation of the results, based mainly on polarimetric readings, has however been shown to be incorrect, the racemisation being accompanied by conversion of α-pinene into dipentene.[¶]

The thermal isomerisation of α-pinene in both the liquid and vapour phase, particularly over copper and other catalysts, has been extensively investigated in recent years,[**] and it has been shown that the main primary products are dipentene (XXV) and allo-*ocimene* (LXXX); under favourable conditions the yield of the latter amounts to 50 per cent. Considerable quantities of *α-pyronene* (LXXXI), b.p. 43°/11 mm., $[\alpha]_D$ + 17° (maleic anhydride *adduct*, m.p. 91°) and *β-pyronene* (LXXXII), b.p. 48–50°/8 mm., $[\alpha]_D$ + 4·5° (maleic anhydride *adduct*, m.p. 163–164°), may also be formed by further isomerisation of the *allo*-ocimene.

---

[*] *J.C.S.* 1884, **45**, 411.

[†] *Ber.* 1877, **10**, 114.

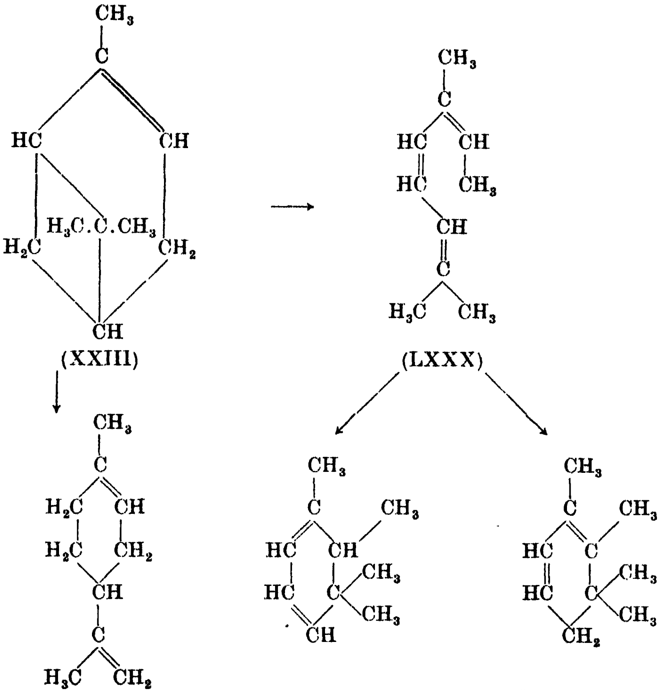
[‡] *Compt. rend.* 1919, **168**, 926.

[§] *Ber.* 1914, **47**, 2078.

[‖] *J. Amer. C.S.* 1927, **49**, 43. Compare Thurber and Roll, *ibid.* 1930, **52**, 786.

[¶] Conant and Carlson, *J. Amer. C.S.* 1929, **51**, 3466; Savich and Goldblatt, *ibid.* 1945, **67**, 2027; Fuguitt and Hawkins, *ibid.* 1947, **69**, 319.

[**] U.S.P. 2,325,422; Arbusov, *Ber.* 1934, **67**, 563; *Chem. Zentr.* 1937, I, 4939; Dupont and Dulou, *Compt. rend.* 1935, **201**, 219; *Brit. Abstr.* A, 1940, II, 182; Charlton and Day, *Ind. Eng. Chem.* 1937, **29**, 92; Goldblatt and Palkin, *J. Amer. C.S.* 1941, **63**, 3517; Fuguitt and Hawkins, *ibid.* 1947, **69**, 319; Savich and Goldblatt, *ibid.* 1945, **67**, 2027; Nikitin, *J. Gen. Chem. Russ.* 1946, **16**, 1475; Swan, *Ind. Chemist*, 1948, **24**, 141.



(XXIII) (LXXX) (XXV) (LXXXI) (LXXXII)

The direct conversion of α-pinene into camphene, in 70 per cent. yield, by refluxing the hydrocarbon over a clay catalyst, has been claimed by Tischenko and Rudakoff.[*]

Unlike dipentene, α-pinene yields little isoprene when passed over a heated platinum spiral.[†] When subjected to the arc discharge it gives a mixture of isoprene, acetylene and ethylene with the deposition of much carbon.[‡]

The action of reducing agents on α-pinene has been investigated very thoroughly. In the early experiments which were made by Berthelot[§] hydriodic acid was used as the reducing agent, whilst Baeyer[‖] used phosphonium iodide. In both these experiments the reaction was carried out at high temperatures

---

[*] *J. Appl. Chem. Russ.* 1933, **6**, 691; compare *Amer. Chem. Abstr.* 1946, **40**, 5775.

[†] Harries and Gottlob, *Annalen*, 1911, **383**, 165, 229; Staudinger and Klever, *Ber.* 1911, **44**, 2213.

[‡] Urbain and Scal, *Compt. rend.* 1919, **168**, 887.

[§] *Bull. Soc. chim.* 1869 [ii], **11**, 19.

[‖] *Annalen*, 1870, **155**, 271.

(270–315°), so that the pinene molecule underwent complete isomerisation. The main product was a hydrocarbon, $C_{10}H_{20}$, b.p. about 160°, which probably consisted essentially of *p*-menthane. Alkaline reducing agents, such as sodamide,[*] have no action on α-pinene. The catalytic hydrogenation of α-pinene to the saturated hydrocarbon, *pinane*, has been discussed in detail on p. 100. Whilst pinane is the normal product obtained by the catalytic hydrogenation of α-pinene, isomerisation to dipentene prior to reduction may also occur under certain conditions. Thus Ipatiev[†], working under high pressure, apparently obtained mainly *p*-menthane. Zelinski[‡] has achieved a simultaneous hydrogenation and dehydrogenation by passing the terpene over heated palladinised asbestos in a current of carbon dioxide, when a mixture of *p*-cymene and pinane is formed. Dehydrogenation occurs also by distillation over platinum black in a current of carbon dioxide at 300°.[§]

Oxidation of α-Pinene

It was early observed that when oil of turpentine was exposed to the air, either in the presence or absence of moisture, the liquid gradually became viscid and, even if water was originally absent or was excluded, drops of water gradually made their appearance. The oxidation of pinene by air (or oxygen) was first studied systematically by Schönbein.[‖] He considered the oxidation to proceed in two stages, the addition of oxygen to the hydrocarbon being followed by the liberation of ozone, which was the actual oxidising agent. This view was controverted by Berthelot[¶] and by Houzeau,[**] who considered the active oxidising agent to be hydrogen peroxide, a view which was shared by Kingzett,[††] who studied the oxidation of α-pinene by oxygen both in the presence and absence of water. He identified formic, acetic and camphoric acids amongst the acids which were formed. The investigations

[*] Lebeau and Picon, *Compt. rend.* 1914, **159**, 72.

[†] *Ber.* 1910, **43**, 3392, 3548.

[‡] *Ibid.* 1925, **58**, 864; see also Linstead, Michaelis and Thomas, *J.C.S.* 1940, p. 1139.

[§] Zelinski and Lewina, *Annalen*, 1929, **476**, 68.

[‖] *J. pr. Chem.* 1851, **52**, 135, 185; **53**, 65; **54**, 74; 1855, **66**, 272; 1858, **75**, 80; *Annalen*, 1857, **102**, 133.

[¶] *Ann. Chim.* 1860 [iii], **58**, 426.

[**] *Compt. rend.* 1860, **50**, 829.

[††] *Inter al.*, *J.C.S.* 1874, **27**, 511; 1875, **28**, 210; *J.S.C.I.* 1910, **29**, 791; 1912, **31**, 265.

of Engler and his collaborators[*] have thrown much light on the mechanism of this oxidation. According to Engler the first product of the oxidation is a peroxide, $C_{10}H_{16}O_2$. This substance is only formed very slowly at 0°, the velocity of the reaction gradually increasing up to 100°, when the rate diminishes, and decomposition occurs at 160°. This peroxide, which may be identical with that described by Susuki (see p. 139), is quite stable in the dark, but it liberates iodine from a solution of potassium iodide, there being one atom of available oxygen per molecule. On exposure to light the peroxide is unstable, oxygen being liberated and, according to Engler, it is this "nascent" oxygen which is the active oxidising agent. Lombard[†] has isolated a polymer, in 53 per cent. yield, by aeration of α-pinene for a month; this product is broken down on acid hydrolysis to give *p*-cymene, terpinolene, and pinol. The autoxidation of α-pinene can be readily inhibited by the addition of anti-catalysts, and Rau[‡] has shown that in the presence of 0·001 per cent. of pyrogallol no oxidation occurs over a period of sixty-two days.

Although it is difficult to separate the primary products of the autoxidation of α-pinene in the absence of water, those formed in the presence of water and more especially in sunlight can be readily isolated. From amongst these the substance *sobrerol* was early recognised. It was probably first obtained pure by Margueron[§] and its composition, $C_{10}H_{18}O_2$, was determined by Blanchet and Sell.[‖] It was, however, for a long time confused with terpin hydrate and was first fully characterised by Sobrero,[¶] who found that it melted at 150°. Later Armstrong[**] and Armstrong and Pope[††] showed that, whilst this was the melting-point of the two optically active forms ($[\alpha]_D$ ± 150°), the *dl*-form melted at 130–131·5°. It was suggested by Armstrong that sobrerol was a glycol, but its constitution was first established as the outcome of the investigations of Wallach on the oxide, *pinol* (Vol. I, p. 436), which is formed from sobrerol by the action of dilute mineral acids. Wallach showed that pinol was represented by

---

[*] Engler and Weissberg, *Über die Autoxidation* (1904). See also Dupont, *Bull. Soc. chim.* 1948, p. 838.

[†] *Bull. Soc. chim.* 1947, p. 251.

[‡] *Ind. For. Rec.* 1924, **11**, 199

[§] *Ann. Chim.* 1797, **21**, 174.

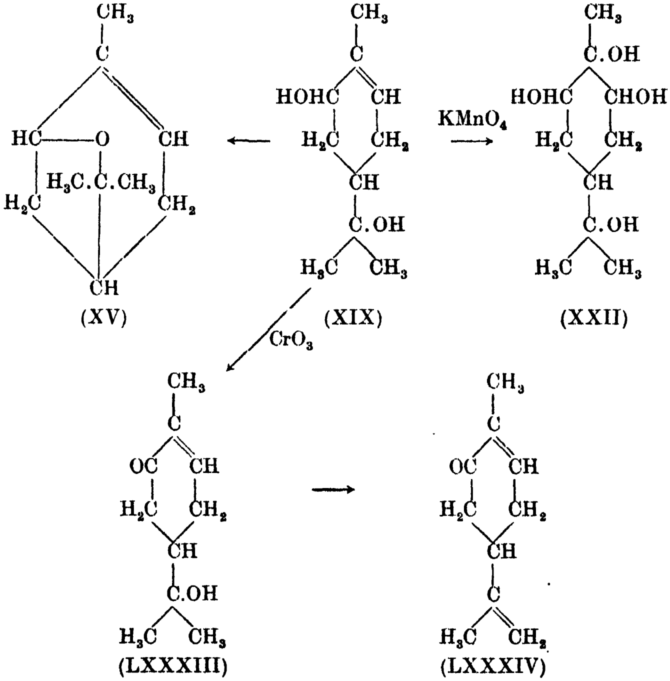
[‖] *Annalen*, 1832, **6**, 267.

[¶] *Ibid.* 1851, **80**, 107; *Compt. rend.* 1851, **33**, 106.

[**] *J.C.S.* 1891, **59**, 311.

[††] *Ibid.* p. 315.

(XV), sobrerol being the corresponding unsaturated glycol (XIX).



(XV) (XIX) (XXII)

(LXXXIII) (LXXXIV)

This formula for sobrerol was confirmed by the experiments of Wagner[*] and Ginzberg,[†] who showed that on oxidation with potassium permanganate p-*menthane*-1 : 2 : 6 : 8-*tetrol* (XXII), m.p. 155·5–156°, was formed, which on further oxidation gave terpenylic and terebic acids, whilst Wallach[‡] obtained by oxidation with chromic acid *hydroxycarvotanacetone* (LXXXIII), from the oxime of which, by the action of dilute sulphuric acid, *carvone* (LXXXIV) was prepared. Ward[§] has shown that *dl*-sobrerol may be obtained by the action of lead tetra-acetate on α-pinene.

In 1913 Blumann and Zeitschel[||] made an interesting addition to our knowledge of the products of the autoxidation of oil of turpentine. It had been observed by Schiff[¶] that oil of turpentine

[*] *Ber.* 1894, **27**, 1644, 2270.

[†] *Ibid.* 1896, **29**, 1195.

[‡] *Annalen*, 1896, **291**, 355.

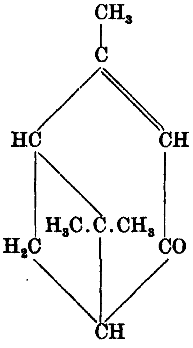
[§] *J. Amer. C.S.* 1938, **60**, 325.

[||] *Ber.* 1913, **46**, 1178.

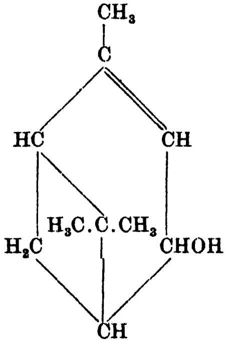
[¶] *Ibid.* 1883, **16**, 2010; *Chem.-Ztg.* 1896, **20**, 361.

which had been exposed to the air gave reactions indicating the presence of an aldehyde. This substance Blumann and Zeitschel succeeded in isolating and found that it was not an aldehyde,[*] but a dicyclic ketone, *verbenone* (LXXXV), the chemistry of which is discussed on p. 232. The corresponding secondary alcohol, *verbenol* (LXXXVI), was also shown to be present. It is of interest to note that, in the formation of this ketone, the ethylenic linkage has escaped oxidation; the reaction is therefore an example of α-methylenic oxidation.

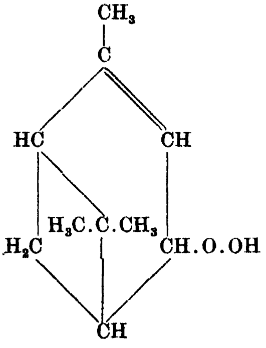
Wienhaus and Schumm[†] have shown that the autoxidation of α-pinene to verbenone and verbenol proceeds very much more rapidly in the presence of catalysts such as osmium; an intermediate *peroxide*, $d_{4°}^{21°}$ 0·9810, $n_D^{21°}$ 1·4885, probably (LXXXVII), has been described by Susuki[‡] which may be identical with that of Engler (p. 137). According to Willstätter and Sonnenfeld,[§] α-pinene reacts with oxygen in the presence of phosphorus to give a crystalline *phosphorate*, which probably has the composition $C_{10}H_{16}P_2O_2$, but analysis was not possible, since it decomposed immediately on exposure to the air.



(LXXXV)



(LXXXVI)



(LXXXVII)

Oxidation of α-pinene with selenium dioxide also results in an attack on a position α to the ethylenic linkage, but contrary to earlier conclusions[‖] it has been shown by Dupont and

---

[*] See, however, p. 224.

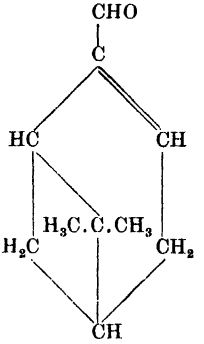
[†] *Annalen*, 1924, **439**, 31.

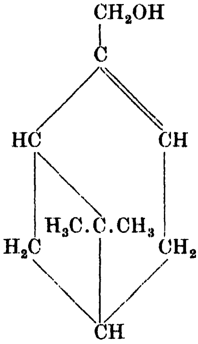
[‡] *Bull. Inst. Phys. Chem. Res. Japan*, 1936, **15**, 70.

[§] *Ber.* 1914, **47**, 2811.

[‖] Schwenk and Borgwardt, *Ber.* 1932, **65**, 1601; Dupont, Allard and Dulou, *Bull. Soc. chim.* 1933 [iv], **53**, 599.

Zacharewicz[*] that the product is not verbenone, but *myrtenal* (LXXXVIII), oxidation having occurred on the methyl rather than on the methylene group. Using a deficiency of selenium dioxide it is possible also to isolate *myrtenol* (LXXXIX), which is therefore the primary product of the oxidation. These authors consider that under certain conditions the autoxidation of α-pinene may produce appreciable amounts of myrtenal, and suggest that the earlier opinion on the selenium dioxide reaction was erroneous owing to the use, for comparative purposes, of "verbenone" which contained a quantity of the aldehyde.


(LXXXVIII)


(LXXXIX)

The ozonolysis of α-pinene has been investigated by Harries and his collaborators. Harries and Neresheimer[†] obtained a liquid ozonide, $C_{10}H_{16}O_4$, but later Harries and Seitz[‡] found that with purified ozone a solid normal ozonide, $C_{10}H_{16}O_3$, is obtained. Either ozonide on decomposition in aqueous solution was said to give pinonic acid, but this is questioned by Spencer, Weaver, Oberright, Sykes, Barney and Elder,[§] who have pointed out an arithmetical error in the analytical figures given by Harries. These workers conclude, from an investigation of the ozonisation of α-pinene in the vapour phase, that α-methylenic oxidation occurs, to give either *verbenone oxozonide* (XC) or *verbenone peroxide ozonide* (XCI), since on decomposition of the product, *pinononic acid* (XCII) is obtained.

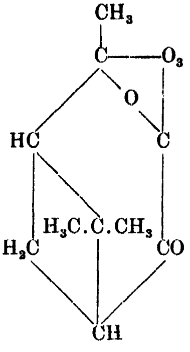
---

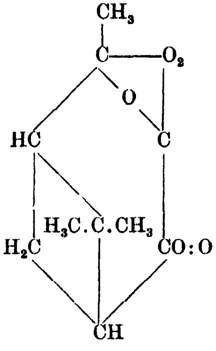
[*] *Compt. rend.* 1934, **198**, 1699; 1935, **200**, 759; *Chem. Zentr.* 1936, II, 2384.

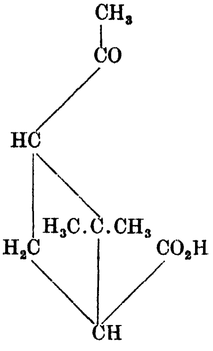
[†] *Ber.* 1908, **41**, 38.

[‡] *Annalen*, 1915, **410**, 22.

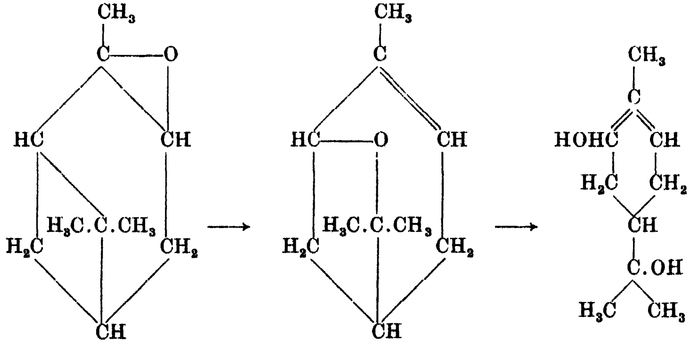
[§] *J. Org. Chem.* 1940, **5**, 610.


(XC)


(XCI)


(XCII)

Prileschaev* examined the action of perbenzoic acid on *l*-α-pinene, which he found to behave normally, yielding l-*pinene oxide* (XCIII), b.p. 102–103°/50 mm., $d^{16°}$ 0·9689, $n_D^{16°}$ 1·4708, $[\alpha]_D$ $-92°$. On hydration with dilute acids ring fission occurs with formation of sobrerol (XV). Nametkin and Jaceva† have since shown the primary hydration product to be pinol (XIX), since if pinene oxide is heated with water at 115–120° pinol is obtained. The conversion of pinene oxide into pinol is only the change of an α- into a γ-oxide. With methyl magnesium iodide, α-pinene oxide gives *methylcampholenol* (XCV),‡ probably derived

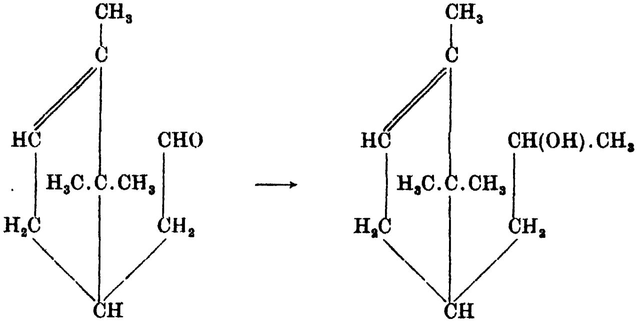

(XCIII) (XIX) (XV)

---

* *Ber.* 1909, **42**, 4814; compare Prileschaev and Verschuk, *J. Russ. Phys. Chem. Soc.* 1929, **61**, 475; Arbusov and Michaelov, *J. pr. Chem.* 1930 [ii], **127**, 1; Delaby and Billuart, *Bull. Soc. chim.* 1943 [v], **10**, 567.

† *J. Russ. Phys. Chem. Soc.* 1924, **55**, 521.

‡ Ritter and Russell, *J. Amer. C.S.* 1936, **58**, 291.



(XCIV) (XCV)

by reaction of the reagent on *campholenic aldehyde* (XCIV), since it has been shown[*] that the oxide may be rearranged to give the aldehyde by treatment with anhydrous metallic halides. For the same reason, derivatives of the aldehyde are obtained when the Reformatsky reaction is carried out on the oxide.

In view of the early theories that hydrogen peroxide was involved in the autoxidation of α-pinene, peculiar interest attaches to the investigation by Henderson and Sutherland[†] of the action of this reagent on α-pinene in acetic acid solution. The oxidation proceeds in a complicated manner, both hydration and molecular rearrangement occurring, the main products isolated being dipentene, α-terpineol, *p*-menthane-1:4:8-triol, borneol and a small quantity of an *aldehyde*, $C_{10}H_{16}O$, identical with that obtained by Henderson and Gray[‡] by the oxidation of α-pinene with chromyl chloride (see below). Of these products the only one to which special attention need be directed is borneol. The formation of this substance, like that of *iso*ketocamphoric acid by the oxidation of pinonic acid (p. 127), involves a molecular rearrangement. Discussion of the mechanism of this reaction is deferred (see p. 159).

The oxidation of α-pinene with mercuric acetate in aqueous solution was first investigated by Balbiano[§] who obtained a hydroxy-ketone, $C_{10}H_{16}O_2$, which he considered to have formula (XCVI), since, on treatment with dilute sulphuric acid, it gave

---

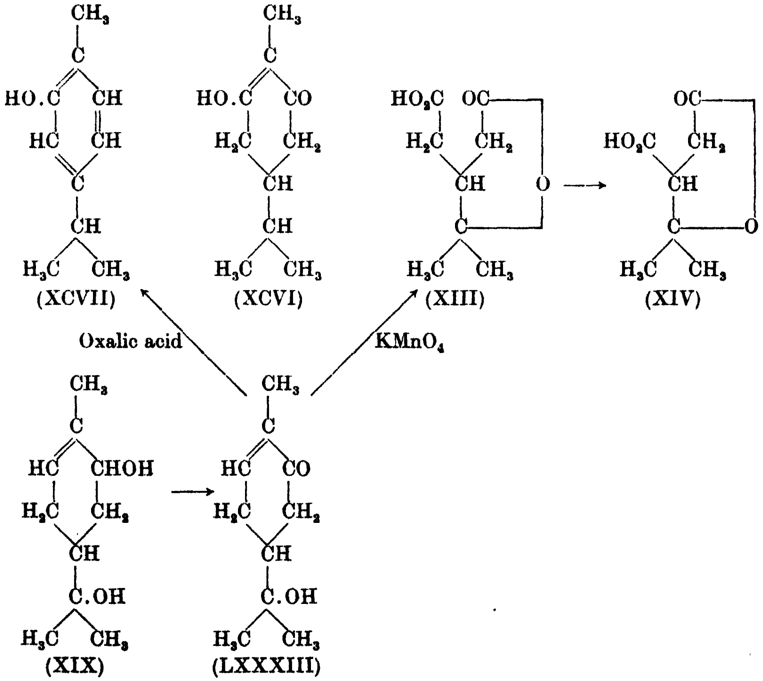
[*] Arbusov, *Ber.* 1935, **68**, 1430; *Chem. Zentr.* 1939, II, 1079.

[†] *J.C.S.* 1912, **101**, 2288.

[‡] *Ibid.* 1903, **83**, 1299.

[§] *Ber.* 1902, **35**, 2994; 1903, **36**, 3575.

carvacrol (XCVII), and, on further oxidation with potassium permanganate, *terpenylic acid* (XIII). A more thorough examination of the products of this reaction was made by Henderson and Agnew[*] and by Henderson and Eastburn,[†] who found that the primary product of the oxidation was *sobrerol* (XIX), which is converted by the further action of mercuric acetate into the hydroxy-ketone described by Balbiano. The constitution of the ketone is not, however, that suggested by Balbiano. Henderson and Agnew proved the ketone to be identical with that prepared by Wallach[‡] by the oxidation of sobrerol with chromic acid (p. 138), namely 8-*hydroxycarvotanacetone* (LXXXIII).



It is of interest to note that Henderson and Eastburn found the sobrerol formed in this oxidation to be optically inactive, although the α-pinene oxidised had a high rotatory power. Balbiano[§] has suggested the use of mercuric acetate for the quantitative estimation of α-pinene, but, in view of the great ease with which this reagent reacts with other terpenes, the method would appear to be of doubtful value.

---

[*] *J.C.S.* 1909, **95**, 289.

[†] *Ibid.* p. 1465.

[‡] *Annalen*, 1896, **291**, 342.

[§] *Ber.* 1915, **48**, 395.

The oxidation of α-pinene with chromic acid was found by Fittig and Krafft[*] to lead to very profound degradation, *terpenylic* (XIII) and *terebic* (XIV) *acids* being formed. The constitution of both these acids has been determined by several independent syntheses.[†] By the use of milder conditions Treibs and Schmidt[‡] were able to obtain verbenone and verbenol by the action of this reagent, the reactions being analogous to those occurring in autoxidation.

Of greater interest are the products which are formed when α-pinene is treated with chromyl chloride. The action of this reagent on the terpene was first investigated by Étard,[§] who found that a vigorous reaction occurred, and he succeeded in isolating, as one of the products, an aldehyde, $C_{10}H_{14}O$, b.p. 205–207°/760 mm. In a renewed study of this reaction Henderson, Gray and Smith[‖] found that when chromyl chloride was allowed to react with the hydrocarbon in carbon disulphide solution a compound of the composition $C_{10}H_{16}, 2CrO_2Cl_2$ was formed, which, on decomposition with water, gave (i) a saturated *aldehyde*, $C_{10}H_{16}O$, m.p. 33°, b.p. 205–207°/755 mm., *semicarbazone*, m.p. 191°; (ii) an unsaturated *ketone*, $C_9H_{14}O$, b.p. 206–207°/774 mm., $d^{20°}$ 0·9678, n_D 1·477, *semicarbazone*, m.p. 226–228°; and (iii) a chlorinated substance, $C_{10}H_{15}OCl$, m.p. 168°. The constitution of these substances was not determined, but it is extremely improbable that they contain the pinene nucleus and they may be derivatives of camphane.

Since the early experiments of Bromeis[¶] on the oxidation of α-pinene with nitric acid, the action of this reagent on the terpene has formed the subject of an extensive series of investigations.[**]

---

[*] *Annalen*, 1881, **208**, 71.

[†] *Inter. al.*, Blaise, *Compt. rend.* 1898, **126**, 349; Schryver, *J.C.S.* 1893, **63**, 1332; Lawrence, *ibid.* 1899, **75**, 531; Simonsen, *ibid.* 1907, **91**, 184. [‡] *Ber.* 1928, **61**, 459.

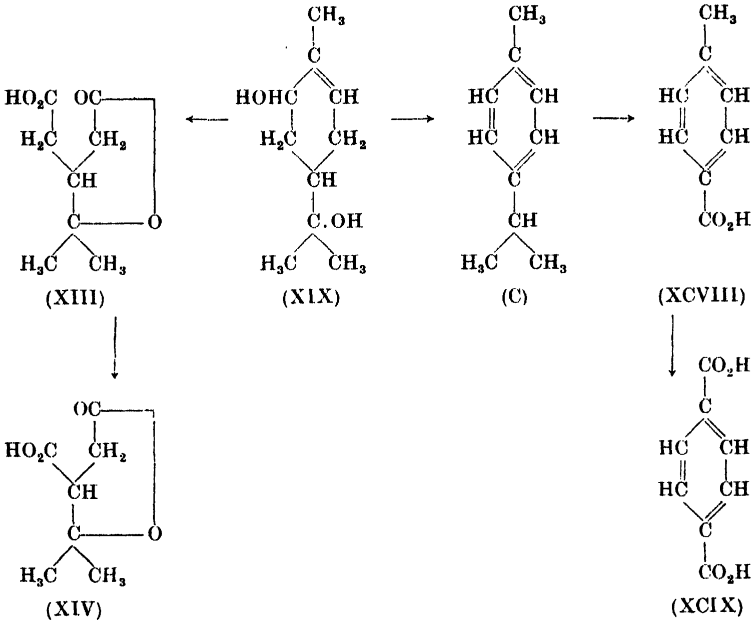
[§] *Ann. Chim.* 1881 [v], **22**, 218; *Compt. rend.* 1893, **116**, 434.

[‖] *J.C.S.* 1903, **83**, 1299; compare Henderson and Smith, *ibid.* 1889, **55**, 45; Henderson and Heilbron, *ibid.* 1908, **93**, 288.

[¶] *Annalen*, 1841, **37**, 297.

[**] *Inter al.*, Rabourdin, *ibid.* 1844, **52**, 391; Cailliot, *Ann. Chim.* 1847 [iii], **21**, 27; Hofmann, *Annalen*, 1856, **97**, 209; Svanberg and Ekman, *J. pr. Chem.* 1855 [i], **66**, 219; Williams, *Ber.* 1873, **6**, 1094; Schreder, *Annalen*, 1874, **172**, 101; Fittig and Bredt, *ibid.* 1881, **208**, 37; Roser, *Ber.* 1882, **15**, 293.

The main products which are formed are terpenylic (XIII), terebic (XIV), *p*-toluic (XCVIII) and terephthalic (XCIX) acids. The formation of these acids is readily explained if we assume that fission of the *cyclo*butane ring first occurs yielding sobrerol (XIX); the glycol is then either oxidised directly to terpenylic and terebic acids or passes into *p*-cymene (C), which is then oxidised to *p*-toluic and terephthalic acids.

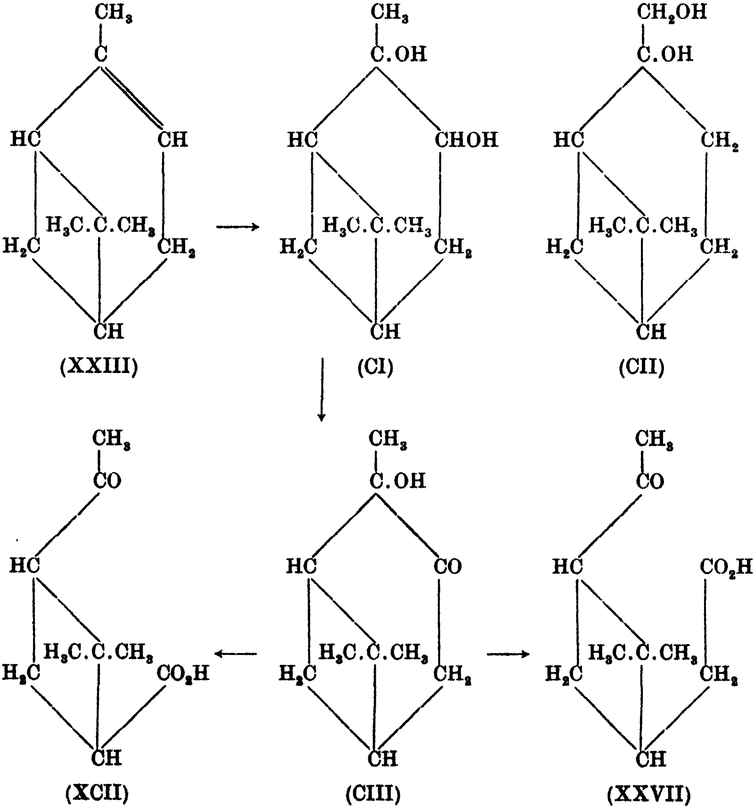


Although reference has been made already in discussing the constitution of α-pinene to some of the products obtained by oxidation with potassium permanganate, it is necessary, in view of its importance, to consider the reaction in greater detail.

Assuming the oxidation to proceed normally, the primary product should be the glycol (CI). In his early experiments, Wagner* obtained a substance, b.p. 145–147°/14 mm., which appeared to be pinene glycol. The oil was, however, undoubtedly a mixture, since it deposited crystals, m.p. 76–78°, which is the melting-point of the glycol (CII) derived from β-pinene (see p. 201). It must be remembered that, at the time of these experiments, "pinene" was assumed to be homogeneous. Wagner's glycol must therefore be regarded as a mixture of the two glycols (CI) and (CII), in which the former probably predominated. On dehydration, it was converted into pinol, together with other substances not investigated in detail. It has only recently been shown* that with neutral permanganate it is possible to obtain

---

* *Ber.* 1888, **21**, 1236; 1890, **23**, 2318; 1894, **27**, 1644, 2270.



(XXIII) (CI) (CII)

(XCII) (CIII) (XXVII)

---

* Slawinski, *Chem. Zentr.* 1932, I, 1091; Kuwata, *J.S.C.I. Japan*, 1936, **39**, 394 B; 1937, **40**, 11 B; Delépine, Horeau and Grandperrin-Harispe, *Ann. Chim.* 1943 [xi], **18**, 250. The conversion of the hydroxy-ketone (CIII) into pinocamphone has been effected by Delépine and Badoche (*ibid.* 1948 [xii], **3**, 573).

the true *α-pinene glycol* (CI) in crystalline form, m.p. 56–57°, accompanied by a ketol, 1-*hydroxypinocamphone* (CIII), m.p. 36° (*dl*-, m.p. 39°). Reduction of the ketol gives a pinene glycol, m.p. 155–160°, which is probably a stereoisomer of (CI). Hydroxypinocamphone is oxidised further only very slowly under the same conditions to give a small yield of pinononic acid (XCII), thus confirming an earlier observation of Wagner and Ertschikowski,[*] but with acid permanganate it is rapidly converted into pinonic acid (XXVII).

dl-Pinonic acid, m.p. 103–104°, b.p. 168°/12 mm., can be prepared in excellent yield if *dl*-pinene is oxidised under the conditions described by Dupont.[†] By the oxidation of *d*- and *l*-α-pinenes the optically active pinonic acids can be prepared.[‡] These were probably first obtained pure by Barbier and Grignard[§] and melt at 68–69°, $[\alpha]_D$ +95·0° (in chloroform solution). The liquid product, which always accompanies the solid acid when it is prepared by oxidation of α-pinene, is probably a mixture of the *cis*- and *trans*-modifications.[‖] It has always been assumed that the crystalline material is the *cis*-isomer, since on oxidation it gives a pinic acid from which a *cis*-norpinic acid may be obtained, but it has recently been shown that the pinic acid thus formed is probably the *trans*-form (see p. 152), and it is therefore not unlikely that the crystalline pinonic acids, described above, also have the *trans*-configuration.[¶] Delépine[**] has investigated the mutarotation which occurs when the acid is treated with alkali, and has shown that this is due not to racemisation but to interconversion of the *cis*- (XXVIIa) and *trans*- (XXVIIb) forms, which probably occurs through the intermediate enol (XXVIIc).

---

[*] *Ber.* 1896, **29**, 881.

[†] *Ann. Chim.* 1923 [ix], **19**, 186.

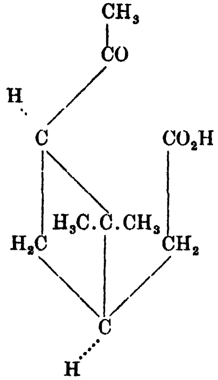
[‡] The so-called *l*-pinonic acid, m.p. 98–99°, $[\alpha]_D$ −21·2°, described by Tiemann (*Ber.* 1896, **29**, 3015), has now been shown to be α-campholonic acid (see p. 120).

[§] *Bull. Soc. chim.* 1910 [iv], **7**, 548; compare Gildemeister and Köhler, *Wallach Festschrift*, p. 426.

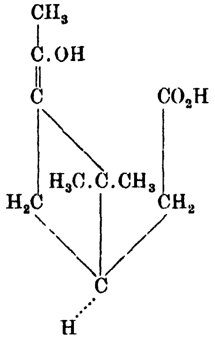
[‖] Perkin and Simonsen, *J.C.S.* 1909, **95**, 1176.

[¶] *cis*-Ring fusion must occur in pinene itself and it has been argued that the pinonic acid formed must also have the *cis*-configuration (XXVIIa), but since the product is never stereochemically homogeneous, this deduction is obviously unsound.

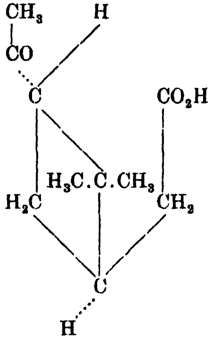
[**] *Bull. Soc. chim.* 1936 [v], **3**, 1369; *Bull. Inst. Pin*, 1936 [iii], 174. In this paper, the *cis*-structure is assumed for the solid acid, but, for the reasons mentioned above, this is probably erroneous.



(XXVIIa)



(XXVIIc)



(XXVIIb)

Pinonic acid can be identified by the preparation of the characteristic *semicarbazone*, described originally by Tiemann and Kerschbaum,[*] *d*- and *l*-forms, m.p. 204°, *dl*-, m.p. 206–207°. From the optically active acids two isomeric *oximes* have been prepared.[†] The lower melting form, known as the *β*-oxime, is derived from the solid *trans*-acid, and melts at 128°, whilst the more sparingly soluble *γ*-oxime, m.p. 190–191°, is derived from the liquid *cis*-acid. The *dl*-*β*-oxime melts at 150°.

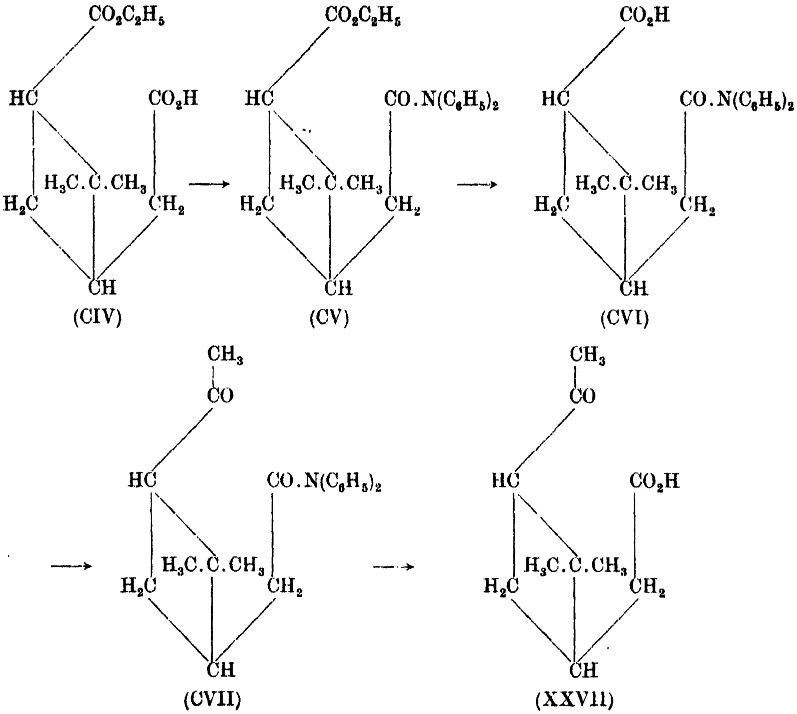
The synthesis of pinonic acid has recently been accomplished by Rao.[‡] For this purpose it was necessary to prepare a derivative of pinic acid in which the primary carboxyl group was protected, whilst the secondary was free. Partial esterification of synthetic pinic acid was unsuccessful, and partial saponification of the di-ester gave only the half-ester (CIV), but this was converted *via* its acid chloride into the *diphenylamide* (CV), which on treatment with sulphuric acid lost only the ester group to give the *acid* (CVI). This was converted, by reaction of its acid chloride with cadmium methyl chloride, into dl-trans-*pinondiphenylamide* (CVII). Removal of the protective grouping with alcoholic alkali gave *dl*-*trans*-pinonic acid, m.p. 103–105°.

---

[*] *Ber.* 1900, **33**, 2664.

[†] Tiemann and Semmler, *Ber.* 1895, **28**, 1346; Baeyer, *ibid.* 1896, **29**, 2786; Wallach, *Annalen*, 1909, **368**, 5; Barbier and Grignard, *Bull. Soc. chim.* 1910 [iv], **7**, 554; Gildemeister and Köhler, *Wallach Festschrift*, p. 426; Delépine, *Bull. Soc. chim.* 1936 [v], **3**, 1369.

[‡] *J. Ind. C.S.* 1943, **20**, 97.


(CIV) (CV) (CVI) (CVII) (XXVII)

dl-Pinonic acid condenses with salicylaldehyde to yield a *styryl* derivative, m.p. 159–161°, but it apparently does not react with other hydroxy aldehydes.*

dl-Ethyl pinonate boils at 147–148°/16 mm.;† the *semicarbazones* of the *d*- and *l*-esters melt at 152–154°.‡

dl-Pinonic acid (XXVII) can be reduced to the corresponding hydroxy acid, dl-*pinolic acid* (CVIII), m.p. 99–100°, by the action of alcoholic potassium hydroxide at 180–200°.§ This hydroxy acid undoubtedly contains the *cyclo*butane ring, since it can be reconverted by oxidation into the parent acid.

By treatment of *dl*-pinonic acid with sulphuric acid (50 per cent.) Baeyer‖ obtained the acyclic ketonic lactone, *homoterpenyl*

---

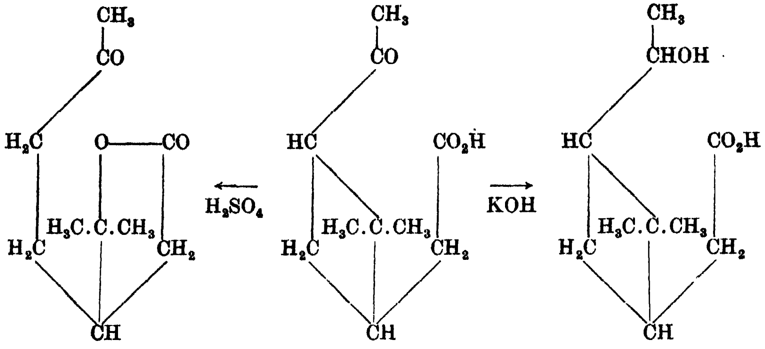
* Fernandez and Mirasierra, *Rec. trav. chim.* 1929, **48**, 852.

† Perkin and Simonsen, *J.C.S.* 1909, **95**, 1174.

‡ Simonsen, *ibid.* 1922, **121**, 2297.

§ Tiemann and Kerschbaum, *Ber.* 1900, **33**, 2665.

‖ *Ber.* 1896, **29**, 326.



(XXXIII) (XXVII) (CVIII)

methyl ketone (XXXIII), the *d*- and *l*-forms of which melt at 47–48° and the *dl*- at 63–65°. From pure *l*-pinonic acid Barbier and Grignard prepared a laevorotatory form with $[\alpha]_D$ $-57{\cdot}4°$, but there is no evidence that this was optically pure. On oxidation with potassium permanganate, homoterpenyl methyl ketone gives terpenylic acid.

Pinononic acid has been obtained as described on p. 140, and by the oxidation of verbenol and verbenone (see p. 233). The *d*- and *l*-forms melt at 128–129°, and the former shows $[\alpha]_D$ $+40°$ in ether (*oxime*, m.p. 178–180°; the m.p. of the *semicarbazone* has been variously reported to lie between 204° and 220°); the *dl*-acid has m.p. 99°. Oxidation with hypobromite gives norpinic acid. Pinononic acid has been synthesised by Guha and Ganapathi[*] from norpinic acid, the monomethyl ester of which was converted into the *acid chloride* (CIX) and condensed with methyl zinc iodide to give *methyl pinononate* (CX) (*semicarbazone*, m.p. 177–178°). Saponification of this ester gave the acid, m.p. 128°. This melting-point, corresponding to that of the optically active acid, is undoubtedly erroneous, since the synthetic product must have been the *dl*-form, which, as mentioned above, has m.p. 99°.[†] The ester was readily cyclised with sodium to give *ketonopinone* (CXI), m.p. 104°.

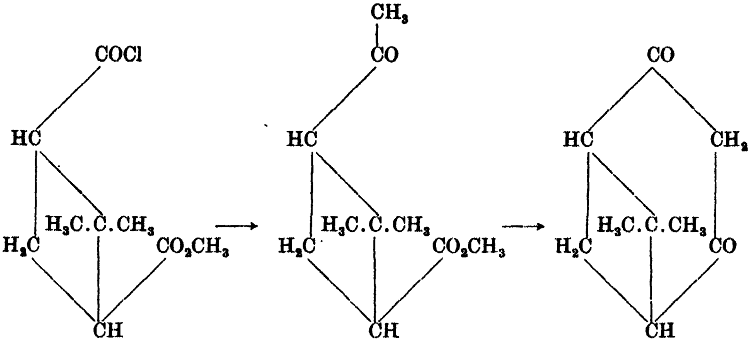
As was first observed by Baeyer[‡] *dl*-pinonic acid is converted quantitatively, by oxidation with sodium hypobromite, into

---

[*] *Ber.* 1936, **69**, 1185.

[†] Compare Komppa and Klami, *Ber.* 1937, **70**, 790, footnote.

[‡] *Ber.* 1896, **29**, 3.



(CIX) (CX) (CXI)

dl-*pinic acid* (XXVIII), m.p. 101- 102·5°, the *d*- and *l*-forms[*] of which have rotatory powers opposite in sign to the parent acids, and melt at 135–136°, $[\alpha]_D$ ± 70·10° (in acetone). Pinic acid does not yield an anhydride. By distillation of the calcium salt Bonsdorff[†] obtained a ketone, b.p. 69–71°/8 mm., which was probably iso*propenyl*cyclo*pentan-2-one*, fission of the *cyclo*butane ring having occurred, but direct proof of its constitution was not obtained.

Pinic acid (XXVIII) reacts readily with bromine to give *bromopinic acid* (XXIX), m.p. 154°, which on digestion with barium hydroxide is converted into the corresponding hydroxy acid, *hydroxypinic acid* (XXX), m.p. 191–193°, *ethyl ester*, b.p. 179°/16 mm.

On oxidation of the hydroxy acid with lead peroxide the *aldehyde* (CXII) is formed,[‡] which has not yet been obtained pure, but which has been characterised by the preparation of the *semicarbazone*, m.p. 188–189°. Oxidation of the aldehyde with potassium permanganate or of the hydroxy acid with chromic acid[§] yields cis-*norpinic acid* (XXXI), m.p. 173–175°.

Until recently, the formation of this acid as the end product in this series of reactions had been taken to indicate that pinic acid, and its bromo- and hydroxy-derivatives, also had *cis*-configurations, but synthetic investigations have shown that this

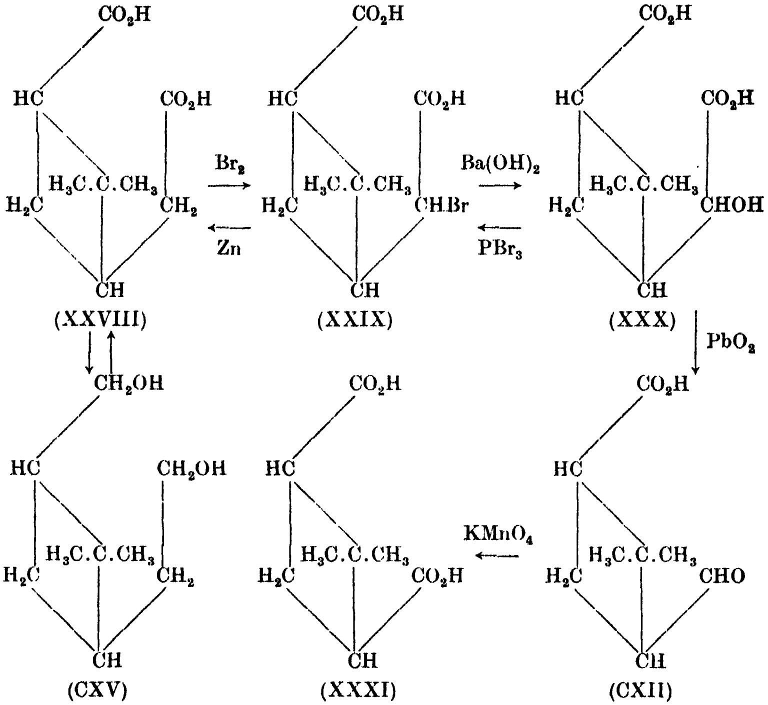
---

[*] Barbier and Grignard, *Bull. Soc. chim.* 1910 [iv], 7, 548.

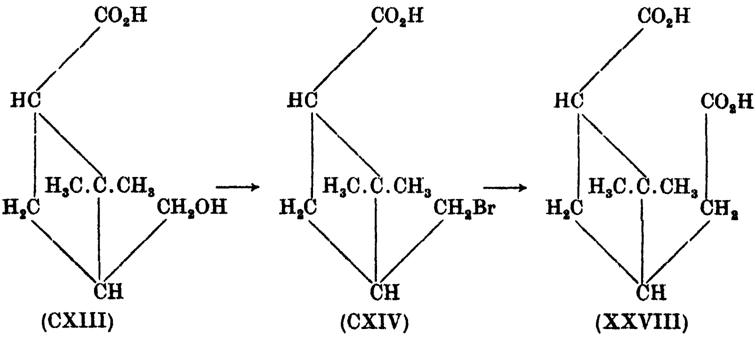
[†] *Ber.* 1911, **44**, 3208.

[‡] Baeyer, *Ber.* 1896, **29**, 1909.

[§] Baeyer, *ibid.* 2787.



supposition is not necessarily correct.* Reduction of *cis*-norpinic anhydride with sodium and alcohol gives the monocarboxylic acid (CXIII) which probably has a *trans*-configuration, since on oxidation it gives *trans*-norpinic acid. The acid (CXIII) was



---

* Guha, Ganapathi, and Subramanian, *Ber.* 1937, **70**, 1505; compare Grandperrin, *Ann. Chim.* 1936 [xi], **6**, 5.

converted through the bromide (CXIV) and nitrile into pinic acid (XXVIII), which could not be obtained crystalline but gave a *dianilide*, m.p. 206–207°, identical with that derived from "natural" pinic acid. Furthermore, *dl*-hydroxypinic acid (XXX) was reconverted with phosphorus tribromide into the bromopinic acid (XXIX), which on treatment with zinc and acetic acid gave a liquid pinic acid, the *diamide* of which, however, melted at 192–193° and was identical with that of the original solid acid.[*] It is deduced from these observations that pinic acid, and its bromo- and hydroxy-derivatives all have the *trans*-configuration, and that the change to *cis*-form occurs only at the last stage, when the *trans*-hydroxypinic acid is oxidised to *cis*-norpinic acid. The hydroxy-acid does not form a lactone, which is additional support for its *trans*-structure. Reduction of crystalline pinic acid with sodium and alcohol gives a *glycol* (CXV), reconverted on oxidation into a product which gives derivatives of the original acid. Since it is known that a similar pair of reactions with *trans*-norpinic acid regenerates the *trans*-acid, it is concluded[†] that these experiments afford additional evidence for the supposition that the crystalline pinic acid is the *trans*-form. The fact that the synthetic pinic acid, and also that obtained from the glycol and from the bromide, all failed to crystallise, suggests that although Guha and his collaborators considered them to be the *trans*-form, and identical with the "natural" solid acid, they were more probably not stereochemically homogeneous. In the opinion of the authors, the main value of this work lies in the clear demonstration that change of configuration can readily occur in such reactions. It may indeed be pointed out that substances such as pinonic, pinononic, pinic, and norpinic acids, all of which carry a carbonyl or carboxyl group adjacent to the ring, would be expected to undergo a change of configuration quite readily, particularly under conditions in which enolisation is facilitated.

cis-Norpinic acid, m.p. 173–175°, is remarkably stable; its configuration was established by Perkin and Simonsen,[‡] since it gives an *anhydride*, m.p. 135°, from which the acid can be regenerated by warming with water. By the action of dilute hydrochloric acid at 180° an equilibrium mixture of *cis*- and *trans*-norpinic acids is obtained, from which the *trans*-acid, which is much more soluble than the *cis*-acid, can be separated by fractional crystallisation; it softens at 137° and melts at 144°.

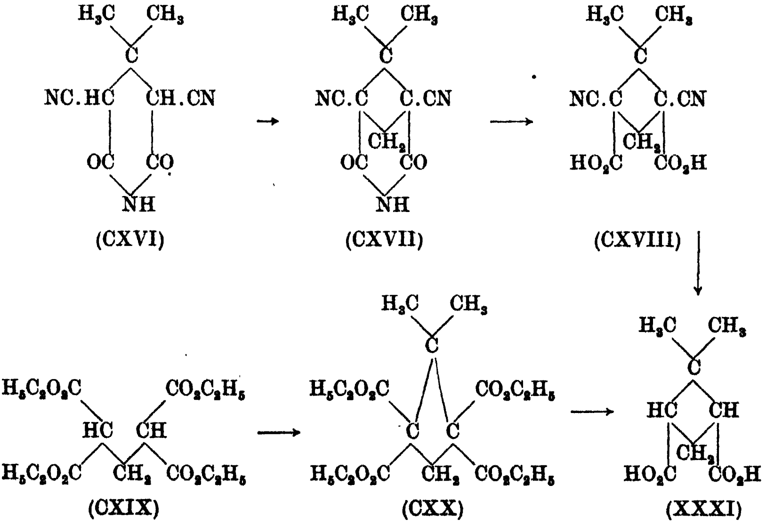
---

[*] Guha and Rao, *Ber.* 1938, **71**, 2663.

[†] Guha, Ganapathi, and Subramanian, *loc. cit.*

[‡] *J.C.S.* 1909, **95**, 1176.

Kerr's elegant synthesis[*] has provided an experimental proof of the correctness of Baeyer's formula for norpinic acid. By the condensation of the sodium derivative of the *cyanoimide* (CXVI) with methylene iodide the bridged *imide* (CXVII) was prepared, from which, by hydrolysis, the *cyano-acid* (CXVIII) and finally *trans*-norpinic acid (XXXI) were prepared; Shoppee and Simonsen[†] converted this into *cis*-norpinic anhydride and *cis*-norpinic acid and were thus able to establish its identity with the acid derived from *dl*-pinonic acid.


(CXVI) (CXVII) (CXVIII)

(CXIX) (CXX) (XXXI)

Guha and Gaind[‡] have also synthesised the *trans*-acid, in small yield, by the condensation of *ethyl propane-ααγγ-tetracarboxylate* (CXIX) with ββ-dichloropropane, to give the *ester* (CXX), followed by saponification and dicarboxylation.

From amongst the oxidation products of α-pinene, Baeyer[§] separated a second ketonic acid, *pinoylformic acid*, $C_{10}H_{14}O_5$

---

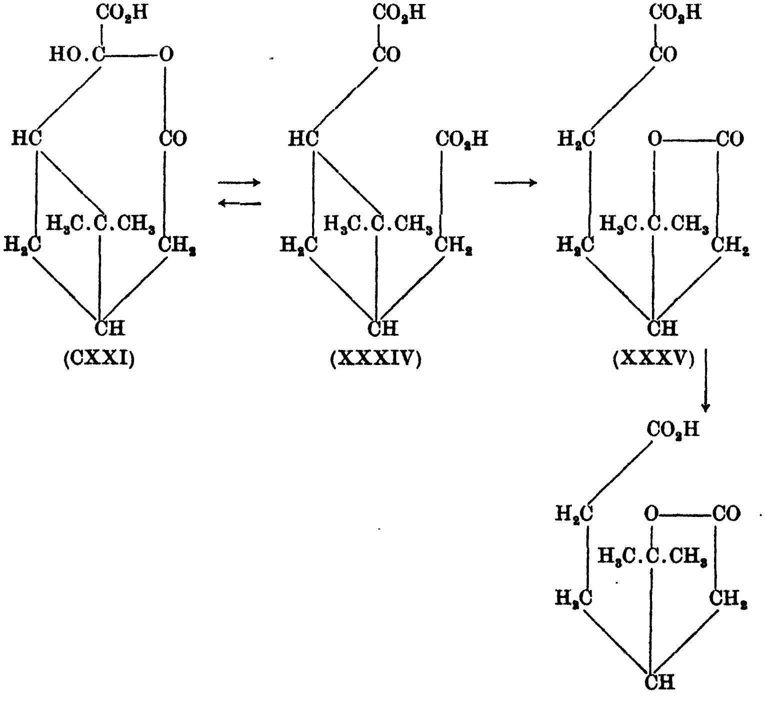
[*] *J. Amer. C.S.* 1929, **51**, 614.

[†] *J.S.C.I.* 1929, **48**, 730.

[‡] *Current Science*, 1934, **2**, 479.

[§] *Ber.* 1896, **29**, 1911.

(XXXIV), by taking advantage of the fact that this acid combines very readily with potassium bisulphite to give a crystalline derivative, from which it can be regenerated by the action of barium hydroxide. According to Ertschikowski,[*] this acid can be obtained also by the oxidation of *dl*-pinonic acid with potassium permanganate; it melts at 78–80° and is somewhat unstable. Although, as is proved by its reactions, pinoylformic acid is undoubtedly the ketonic dibasic acid represented by (XXXIV), it behaves on titration as a lactone and exists therefore also in the tautomeric form (CXXI). The *phenylhydrazone* melts at 192·5°. The constitution of pinoylformic acid is conclusively proved by its oxidation with potassium permanganate to pinic acid, and by its conversion on boiling with dilute sulphuric acid into *homoterpenylformic acid* (XXXV), m.p. 126–129°, which, on oxidation with lead peroxide, gives *homoterpenylic acid* (XXXVI),


(CXXI) (XXXIV) (XXXV) (XXXVI)

---

[*] *Ber.* 1899, **32**, 2079.

m.p. 98–101°, which has been synthesised by Simonsen.[*] On reduction with sodium amalgam, pinoylformic acid yields the corresponding hydroxy acid, m.p. 130–133°.[†] The nature of the products formed on oxidation with sodium hypobromite have been discussed on p. 123.

Molecular Rearrangements of α-Pinene and Related Compounds

Before proceeding to give an account of the remaining reactions of α-pinene it will be convenient to discuss here one of the most important properties shown, not only by α-pinene and its derivatives, but also by other dicyclic terpenes, namely the great tendency which they exhibit to isomerise to substances having a different ring structure. The following may be regarded as typical examples of this type of reaction:

(i) the hydration of α-pinene (XXIII) to yield *borneol* (CXXII) and *fenchyl alcohol* (CXXIII),

(ii) the conversion of α-pinene into *bornyl chloride* (CXXIV) by the action of hydrogen chloride,

(iii) the dehydration of iso*borneol* (CXXII) to *camphene* (CXXV),

(iv) the conversion of *camphene hydrochloride* (CXXVI) into iso*bornyl chloride* (CXXIV).

These changes are shown schematically on p. 157, the reaction with α-pinene being more readily understood if the formula for the hydrocarbon be written as in (XXIIIa) and (XXIIIb).

Wagner[‡] recognised that a molecular rearrangement was involved in the formation of bornyl chloride from α-pinene, and he suggested that a simple analogy was to be found in the dehydration of the alcohol (CXXVII) to the hydrocarbon (CXXVIII), which, by the action of hydrogen chloride, gives the chloride (CXXIX), the isomeric chloride (CXXIXa) possibly having a transitory existence.

$$\underset{\text{(CXXVII)}}{(H_3C)_3C.CHOH.CH_3} \rightarrow \underset{\text{(CXXVIII)}}{(H_3C)_2C{:}C(CH_3)_2} \rightarrow \underset{\text{(CXXIXa)}}{(H_3C)_2CH.CCl(CH_3)_2}$$

$$\rightarrow \underset{\text{(CXXIX)}}{H_3C.CHCl.C(CH_3)_3}$$

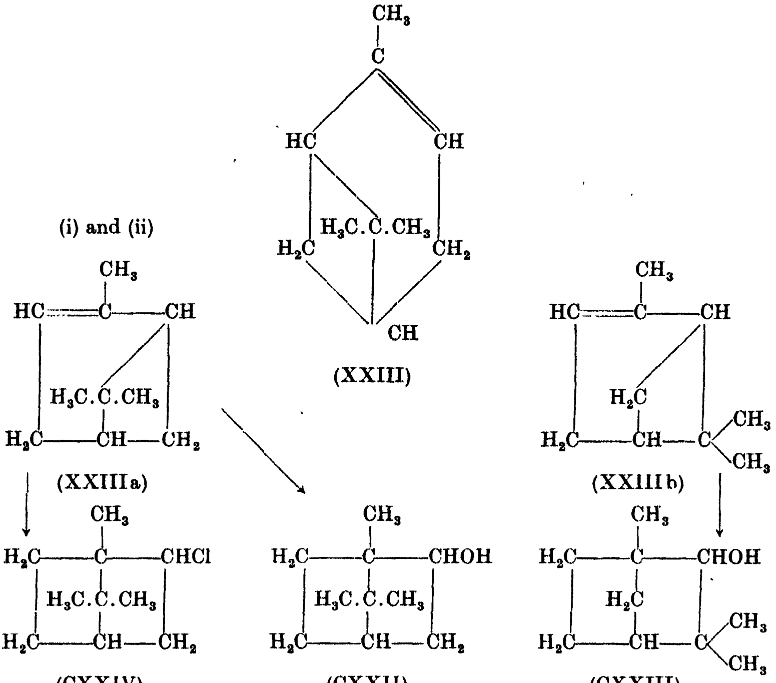
---

[*] *J.C.S.* 1907, **91**, 190.

[†] Baeyer, *Ber.* 1896, **29**, 2789.

[‡] *J. Russ. Phys. Chem. Soc.* 1899, **31**, 690.

(i) and (ii)



(XXIII)

(XXIIIa)

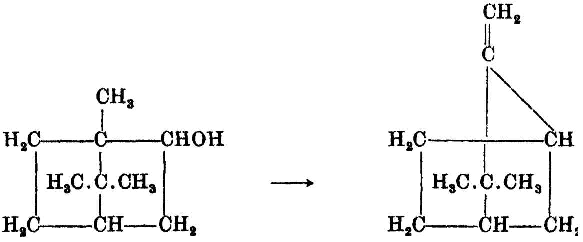
(XXIIIb)

(CXXIV)

(CXXII)

(CXXIII)

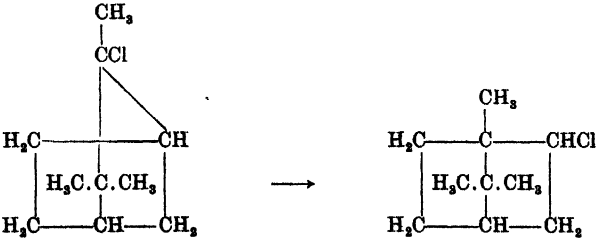
(iii)



(CXXII)

(CXXV)

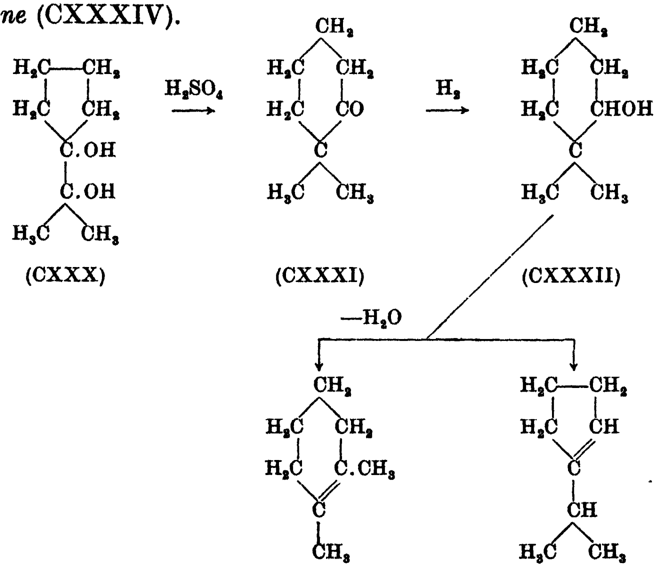
(iv)



(CXXVI)

(CXXIV)

Other and more instructive analogies have been observed by Meerwein,* of which the following examples offer sufficient illustration. 1-iso*Propyl*cyclo*pentane*-1 : *α-diol* (CXXX) yields on treatment with dilute sulphuric acid 1 : 1-*dimethyl*cyclo*hexan*-2-*one* (CXXXI). The dehydration of the *alcohol* (CXXXII) prepared by the reduction of the latter gives rise to a mixture of 1 : 2-*dimethyl*-Δ^1-cyclo*hexene* (CXXXIII) and iso*propyl*-Δ^1-cyclo*pentene* (CXXXIV).



(CXXX) (CXXXI) (CXXXII)

(CXXXIII) (CXXXIV)

The mechanism involved in these pinacon-pinacolin transformations has been much discussed. In the conversion of *iso*borneol (CXXII) into camphene (CXXV) it has been assumed that *tricyclene* (CXXXV) is an intermediate product,† the reaction being formulated as shown on p. 159.

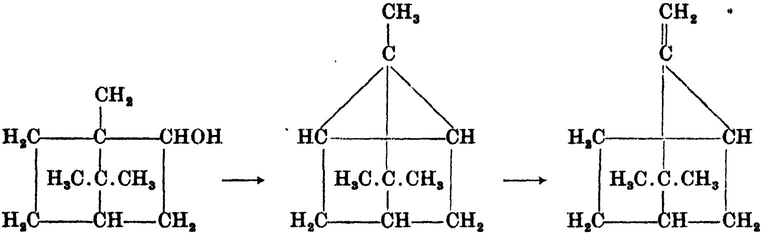
The transitory existence of tricyclic derivatives can also be used to explain the other reactions given above. Meerwein and Emster‡ have shown conclusively that in the case of the *iso*borneol-camphene change the reaction cannot proceed in this manner, since tricyclene is perfectly stable under conditions which convert *iso*borneol into camphene. Further evidence was

---

* *Annalen*, 1910, **376**, 152; 1914, **405**, 129; 1918, **417**, 255. See also *Ann. Reports*, 1933, **30**, 181; 1939, **36**, 195.

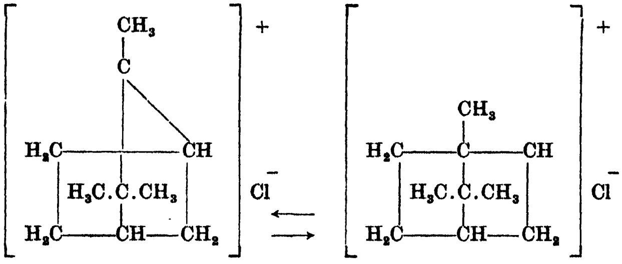
† Compare Ruzicka, *Helv. Chim. Acta*, 1918, 1, 130.

‡ *Ber.* 1920, **43**, 1815; cf. Lipp, *ibid.* 769.



(CXXII) (CXXXV) (CXXV)

furnished by a study of the velocity of the conversion of camphene and tricyclene into *iso*bornyl chloroacetate by the action of chloroacetic acid. The esterification of camphene proceeds with a far greater velocity than that of tricyclene, which could obviously not be the case if tricyclene was an intermediate stage in the reaction. Meerwein considers that the isomerisation is preceded by ionisation, the actual molecular rearrangement occurring in the cation, evidence in support of this view being afforded by a study of the velocity of the change camphene hydrochloride (CXXVI) to *iso*bornyl chloride (CXXIV).

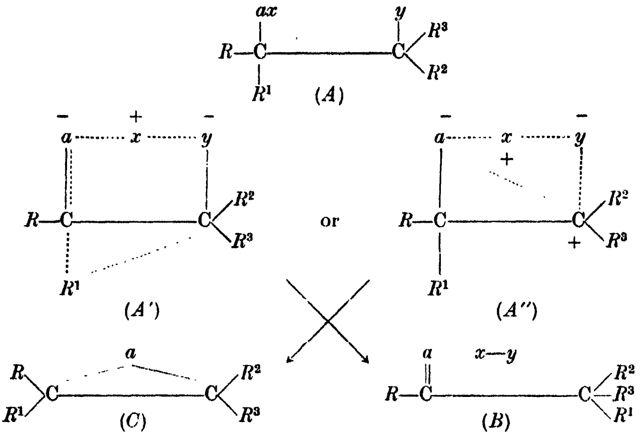


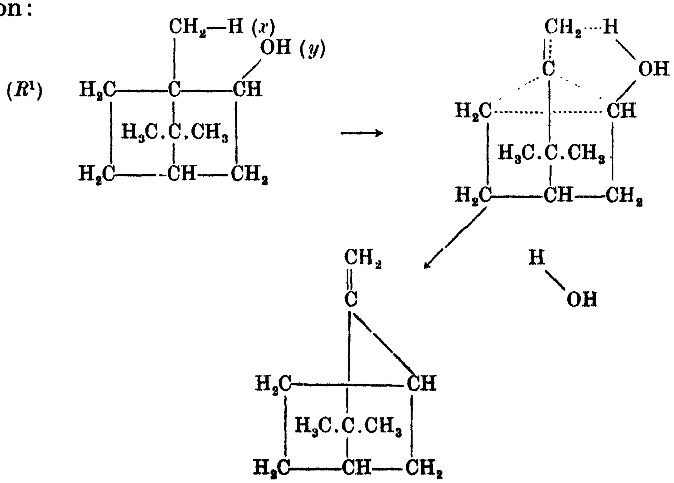
(CXXVI) (CXXIV)

We are, however, indebted to Robinson[*] for a precise and adequate correlation of these changes with the pinacon-pinacolin transformation, which would appear to have been overlooked by other investigators. In his original communication the symbolism of partial valencies was used, the dehydration of a pinacon (*A*) to a pinacolin (*B*) being directly correlated with the Wagner or borneol-camphene rearrangement. In the representation (*A*), R, R^1, R^2, R^3 are assumed to be neutral groups, whilst a is a divalent atom or group and x, y are monovalent atoms or groups of such a nature that there is a tendency to form a compound xy.

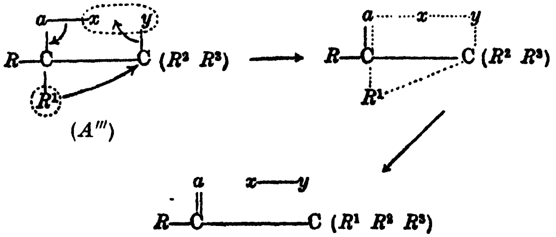
[*] *Mem. Manchester Phil. Soc.* 1921, **64**, No. 4, 1.

If it be assumed that x is electropositive in character and y electronegative and that they become attached by a partial valency, then there arises conjugation and the conditions represented by (A') and (A''). Now if xy separate from (A'') by compound formation a three-membered ring may be formed, as in (C), whilst the separation of xy from (A') will give (B). This latter reaction is the ordinary pinacon-pinacolin reaction, where a is oxygen, x hydrogen and y is hydroxyl. To illustrate this, the borneol-camphene change is shown by the following representation:

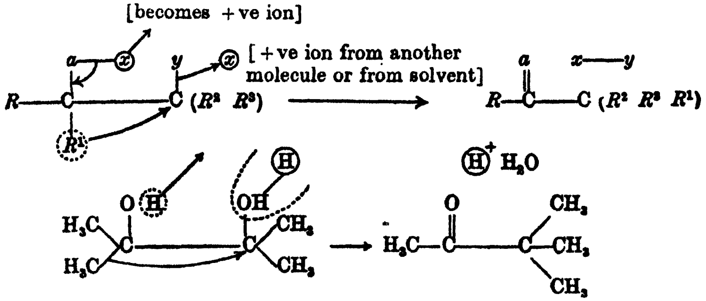




With the elaboration of the electronic theories of valency, which we owe mainly to Lapworth and Robinson, the expression (*A*) may be written as in (*A‴*) where "———" corresponds to two electrons, the intermediate bodies postulated, (*A′*) and (*A″*), being identical if "........." be assumed to correspond to one electron.*



A further advance was made in theoretical interpretation by the suggestion of Lapworth that the reaction in such cases is probably not direct, but takes place by an ionic mechanism. This theory may be represented as shown below:

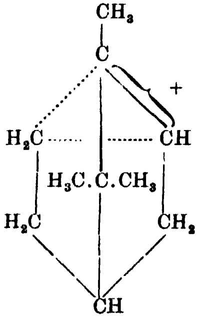


The Robinson theory, with the ionic extension suggested by Lapworth, provided a simple explanation of the Wagner reaction and had the valuable additional merit that it co-ordinated it with the well-known pinacon-pinacolin rearrangement. In its essentials, the theory has remained unchanged, though in accordance with more recent electronic concepts it has undergone slight modifications in detail. The mesomeric structure (CXXXVI), suggested by Ingold† to represent the intermediate ion in the camphene-borneol change, can be regarded as the modern equivalent of the partial valency formula.

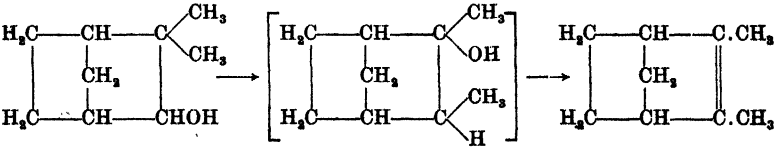
---

* Compare Lapworth, *J.C.S.* 1922, **121**, 416; Kermack and Robinson, *ibid.* p. 427.

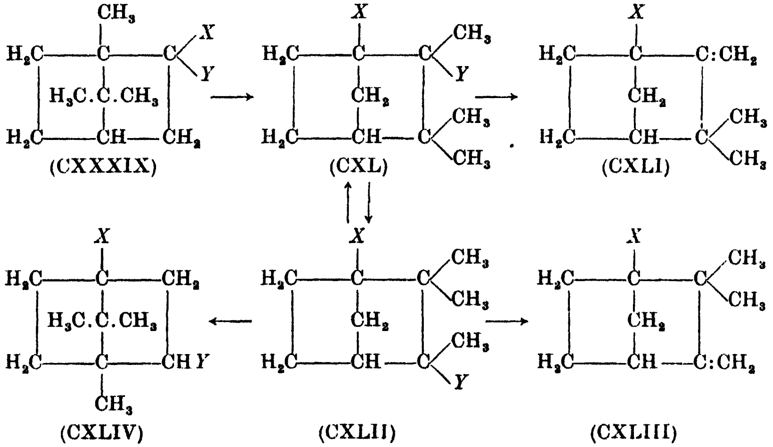
† *Ann. Reports*, 1939, **36**, 197; compare Nevell, de Salas, and Wilson, *J.C.S.* 1939, p. 1188.


(CXXXVI)

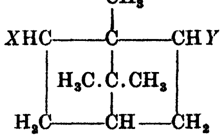
In the example given on p. 158 it was shown that dehydration of the *cyclo*hexane derivative (CXXXII) gives two products. In the formation of one of these (the *iso*propyl*cyclo*pentene) the pinacolic change results in a modification of ring structure, and this is analogous to the terpene transformations already considered; the dimethyl*cyclo*hexene, however, is derived by a pinacolic change without ring isomerisation. In the terpene field an example of this latter type is provided in the dehydration of *camphenilol* (CXXXVII) to *santene* (CXXXVIII), but until comparatively recently it has not been realised that this so-called "camphene change of the second type" is of frequent occurrence. This reaction, which is now generally described under the term "Nametkin change", has been studied by Nametkin, Bredt, Houben, Lipp and others. Specific examples will be found in the sequel (pp. 292, 304, 344, etc.), but it is desirable at this stage to give a brief indication of the manner in which isomerisation may arise by a combination of the Wagner and Nametkin rearrangements. For purposes of illustration, a 2:2-disubstituted camphane (CXXXIX), where $X = H$, CH_3, CO_2H, etc., and $Y = OH$, OAc,

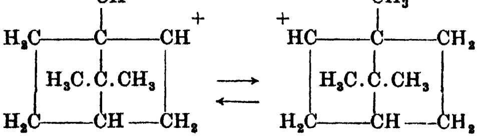

(CXXXVII) (CXXXVIII)

Cl, Br, etc., will be taken as a general example. A Wagner rearrangement on such a substance would normally proceed through the intermediate *iso*camphane derivative (CXL), which by loss of H*Y* would form the 1-substituted camphene (CXLI). Under certain conditions, however, the intermediate (CXL) may undergo a Nametkin change to give (CXLII), and the subsequent loss of H*Y* results in the formation of the 4-substituted camphene (CXLIII); alternatively, (CXLII) may undergo a Wagner rearrangement and yield the 2:4-disubstituted camphane (CXLIV). Compounds of the latter type had previously been formulated as 2:6-derivatives (CXLIVa), and, since the Wagner rearrangement would not account for such an isomerisation, Meerwein and Montfort* had concluded that the direct migration of a substituent occurred, from the 2- to the 6-position; the racemisation of bornyl chloride, for example, was thought to proceed by a 2–6 isomerisation within the bornyl ion (CXLV). It is difficult, however, to provide any theoretical justification for such an


(CXXXIX) (CXL) (CXLI)

(CXLIV) (CXLII) (CXLIII)


(CXLIVa)

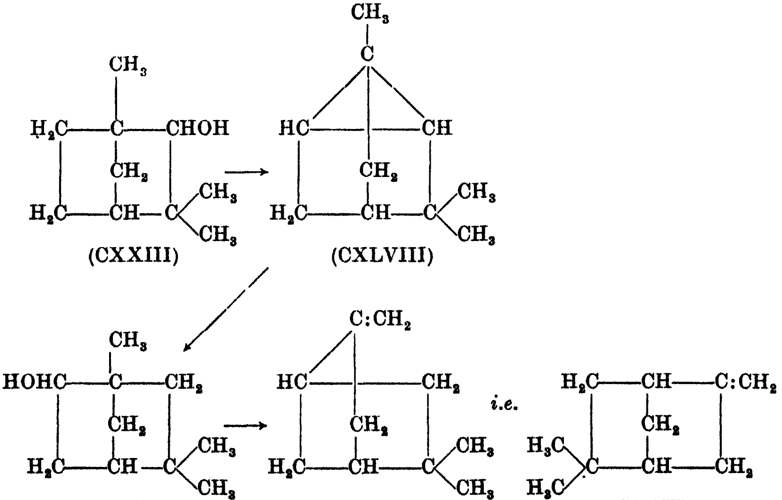

(CXLV)

---

* *Annalen*, 1924, **435**, 213.

isomerisation, and the discovery that these changes result in a migration from the 2- to the 4-position has eliminated the necessity of postulating such a 2–6 ionic interchange, and has led to the provision of a reasonable explanation of the observed facts. It is important to note that the substituted camphenes (CXLI) and (CXLIII) differ not only structurally, but also in configuration, and if $X = H$ they become true enantiomorphs. Similarly, (CXXXIX; $X = H$, $Y = Cl$) and (CXLIV; $X = H$, $Y = Cl$) represent enantiomorphous forms of bornyl chloride. The Nametkin change is therefore able to account also for the facile racemisation shown by bornyl chloride and camphene.

The position is not yet so clear in the fenchane series, where dehydration of fenchyl alcohol (CXXIII) can give rise to a hydrocarbon such as β-fenchene (CXLVI), which cannot be derived from this alcohol by any normal Wagner or Nametkin change. The hydrocarbon can, however, be derived by Wagner change from *iso*fenchyl alcohol (CXLVII), and it is therefore necessary to consider possible mechanisms for the interconversion of these two structurally isomeric alcohols. *iso*Fenchyl alcohol could evidently be formed from fenchyl alcohol by a migration of the 2–6 type originally considered in the camphane series; alternatively, the transformation may be assumed to occur through



the intermediate formation of cyclo*fenchene* (CXLVIII). The latter hypothesis is comparable with the postulation of tricyclene as an intermediate in the camphene-borneol change, but differs from it in one very important respect, in that the properties of *cyclo*fenchene, unlike those of tricyclene, are not incompatible with such a reaction mechanism. It has already been pointed out that it is difficult to give any theoretical explanation for the concept of an ionic interchange between the 2- and 6-positions, and the alternative view is therefore more attractive, though it is recognised that further investigations in this field are very desirable.*

General Reactions of α-Pinene

On hydration with dilute mineral acids or with organic acids α-pinene yields products of two distinct types: (i) by fission of the *cyclo*butane ring with formation of monocyclic alcohols and hydrocarbons, and (ii) by molecular rearrangement and conversion into derivatives of camphane and fenchane. By the choice of suitable conditions either the one or the other of these two reactions can be made to predominate. Owing to the technical importance of the products which are formed, the hydration of α-pinene has been exhaustively studied, and it is only possible to give here a general outline of these investigations. In the majority of cases pure α-pinene free from β-pinene has not been used, and there has been considerable discussion as to whether both hydrocarbons react in the same manner. This problem cannot be regarded as definitely elucidated, but it seems probable that, whereas the products from the two hydrocarbons are qualitatively the same, they differ quantitatively, α-pinene being more slowly hydrated than β-pinene and giving higher yields of monocyclic derivatives.† The mechanism of the acid-catalysed isomerisation of α-pinene has been discussed by Mosher.‡

---

* Compare Hückel, *Theoretische Grundlagen der Organischen Chemie*, 5th ed., 1944, Vol. I, pp. 320–329, 334, 341–342. The mechanisms of rearrangement in the camphane and fenchane series have also been discussed by Böeseken (*Rec. trav. chim.* 1935, **54**, 101), but some of his conclusions are vitiated by incorrect formulations of certain reaction products.

† See *inter al.*, Barbier and Grignard, *Bull. Soc. chim.* 1909 [iv], **5**, 512, 519; Dupont, *Chim. et Ind.* 1922, **8**, 855; Grignard and Stratford, *Bull. Soc. chim.* 1923 [iv], **33**, 531; Delépine, *Compt. rend.* 1924, **178**, 2087; 1924, **179**, 980; Austerweil, *Bull. Soc. chim.* 1926 [iv], **39**, 690, 1732; 1927 [iv], **41**, 1088, 1507.

‡ *J. Amer. C.S.* 1947, **69**, 2139.

Whilst pinene[*] is only very slowly acted upon by dilute sulphuric acid, with the concentrated acid a complex reaction takes place with the formation of limonene (*d*- or *l*- depending upon the rotatory power of the pinene used), dipentene, terpinolene, terpinene, camphene, and *p*-cymene.[†] Treatment of the reaction mixture with an excess of an alcoholic solution of potassium hydroxide at 150° under pressure results in the formation of appreciable quantities of borneol and fenchyl alcohol. If a large proportion of mineral acid is used, it has been observed by Brooks and Humphrey[‡] that polymerisation takes place with the formation of hydrocarbons having a high molecular weight; α-*dipinene*, one of the products of this reaction, has been studied by Dulou.[§] With sulphuric acid in alcoholic solution at the ordinary temperature, α-terpineol or its ether is obtained in a good yield,[‖] although, if the mixture is heated, monocyclic terpenes result.[¶] With dilute nitric, hydrochloric, hydriodic and phosphoric acids pinene gives mainly terpin hydrate,[**] a product which is formed also by the action of dilute sulphuric acid if the hydrocarbon and the acid are allowed to remain in contact for a considerable period under conditions allowing a large reaction surface.[††]

During recent years the use of organic acids for the hydration of pinene has found increasing application, since the reaction can be more readily controlled. The hydration proceeds in exactly the same manner as with mineral acids, so that only brief mention is required. Kharasch and Reynolds[‡‡] have shown that the yield of bornyl ester depends on the ionisation constant of the organic acid employed, and in certain cases may be improved by the incorporation of phenol in the reaction mixture. The presence of an amide, on the contrary, inhibits esterification, and leads to a good yield of limonene. According to Reisman[*] anhydrous formic acid gives a mixture of limonene, dipentene, terpinene, terpinolene, diterpenes, terpinyl formate and bornyl formate, whilst with acetic acid similar products are formed, although under suitable conditions terpinyl acetate can be made the main product.[†] α-Terpineol can be conveniently prepared by the action of benzenesulphonic acid.[‡]

---

[*] The general term "pinene" is used here to indicate a mixture of α- and β-pinenes.

[†] Armstrong and Tilden, *Ber.* 1879, **12**, 1752; Bouchardat and Lafont, *Compt. rend.* 1887, **105**, 1177; 1897, **125**, 113; Wallach, *Annalen*, 1887, **239**, 35; Charlton and Day, *Ind. Eng. Chem.* 1937, **29**, 92.

[‡] *J. Amer. C.S.* 1918, **40**, 844.

[§] *Bull. Inst. Pin*, 1931, 159, 173, 199, 219; cf. Ritter and Sharefkin, *J. Amer. C.S.* 1940, **62**, 1508.

[‖] Flavitzky, *Ber.* 1879, **12**, 1406, 2354; 1887, **20**, 1957; Godlewski, *J. Russ. Phys. Chem. Soc.* 1899, **31**, 201; Treibs, *Ber.* 1937, **70**, 589.

[¶] Wallach, *Annalen*, 1885, **227**, 283; **230**, 262; Smirnov, *J. Russ. Phys. Chem. Soc.* 1909, **41**, 996.

[**] Wiggers, *Annalen*, 1840, **33**, 359; 1846, **57**, 247; Hempel, *ibid.* 1876, **180**, 73; Tilden, *J.C.S.* 1879, **35**, 262; Flavitzky, *Ber.* 1879, **12**, 1022, 1406; Aschan, *Bidrag til Kännedom af Finland's Natur och Folke*, 1918, **77**, 1.

[††] Beilstein, *Handbuch der Organischen Chemie*, 4th ed. v, 152.

[‡‡] *J. Org. Chem.* 1944, **9**, 148.

The action of chlorine on α-pinene has formed the subject of numerous investigations, the earliest being due to Deville[§] and Naudin.[‖] Owing to the complex manner in which the reaction proceeds, the actual nature of all the products of the reaction has not yet been determined. The primary product is probably the *dichloride* (CXLIX); this substance is, however, too unstable to permit of isolation, and even at low temperature decomposes with the liberation of hydrogen chloride. The most recent investigations of this reaction have been made by Aschan[¶] and by Brus.[**] Even if water is rigidly excluded and the reaction carried out at − 15°, Aschan found it to be most complex. He succeeded in isolating a dichloride, *bornyl dichloride* (2:6-*dichlorocamphane*) (CL), m.p. 173–174°, a liquid dichloride of undetermined constitution, and *bornyl chloride* (CLI).

The latter is probably a secondary product, being formed by the action of hydrogen chloride, generated by the decomposition of (CXLIX), on unattacked α-pinene. It is not known whether the bornyl dichloride is formed directly by the rearrangement of pinene dichloride, which Aschan assumed to be the case, or by the chlorination of bornyl chloride. It would appear not improbable that both reactions occur simultaneously, and that the liquid dichloride is actually a mixture of stereoisomeric bornyl dichlorides. Brus obtained very similar results and he prepared also a dichloride, m.p. 170–171°, bornyl chloride, together with more highly halogenated products. Since his dichloride crystallised in the monoclinic system and that of Aschan in the orthorhombic, he did not regard them as identical, but until direct comparison of the two substances has been made, the non-identity cannot be regarded as established. The constitution of the dichloride is proved by its conversion into tricyclene (p. 333) by the action of sodium.

---

[*] *Bull. Soc. chim.* 1927 [iv], **41**, 94; compare Lafont, *ibid.* 1888 [ii], **49**, 323; Delépine, Reisman and Suan, *ibid.* 1930 [iv], **47**, 966.

[†] Bouchardat and Lafont, *Compt. rend.* 1898, **126**, 755; Zeitschel, *G.P.* 204163; *G.P.* 67255; Guha and Roy, *J. Ind. Inst. Sci.* 1941, **23** A, 208; compare Paillard and Tempia, *Helv. Chim. Acta*, 1931, **14**, 1314.

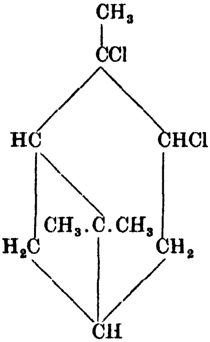
[‡] Barbier and Grignard, *Bull. Soc. chim.* 1909 [iv], **5**, 512, 519; Germuth, *Amer. J. Pharm.* 1927, **99**, 402.

[§] *Annalen*, 1841, **37**, 190.

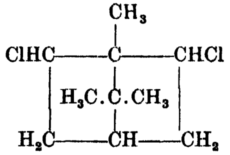
[‖] *Bull. Soc. chim.* 1882 [ii], **37**, 111.

[¶] *Öfvers. Finska Vet. Soc.* 1915, **57**, 1; *Ber.* 1928, **61**, 38.

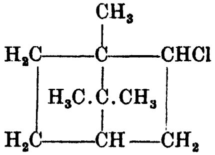
[**] *Compt. rend.* 1925, **180**, 1507; *Brit. Chem. Abstr.* 1931, p. 230; compare Gallas and Montañés, *Anal. Fís. Quím.* 1930, **28**, 1163.



(CXLIX)



(CL)



(CLI)

The bromination of α-pinene proceeds in an exactly analogous manner to the chlorination, and gives a mixture of *bornyl bromide* (CLIII) and *bornyl dibromide* (CLIV), although the tendency for hydrogen bromide to be eliminated and for *p*-cymene to be formed is greater. The early experiments of Deville,[*] Oppenheim,[†] Barbier[‡] and Kekule[§] did not lead to the separation of any crystalline derivatives, but the isolation of *p*-cymene either by direct distillation or after treatment with bases was of fundamental theoretical importance in showing the relationship of α-pinene to the aromatic hydrocarbons. Later investigators[‖] were concerned mainly with quantitative estimations of the absorption of bromine, but Flavitzky possibly prepared true α-pinene *dibromide* (CLII), which he describes as an oil, $d_{0^\circ}^{4^\circ}$ 1·5493, n_D 1·5475, $[\alpha]_D$ +30·5°, which did not crystallise at − 30°. This substance was prepared by bromination in acetic acid solution. A crystalline *dibromide*, m.p. 169–170°, together with *bornyl bromide*, m.p. about 90°, was obtained by Wallach,[*] Wallach considered the dibromide to be a true pinene derivative, but this was shown by

---

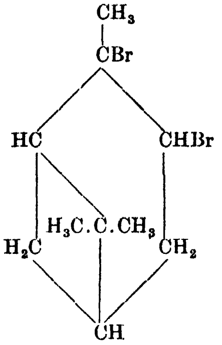
[*] *Annalen*, 1841, **37**, 191.

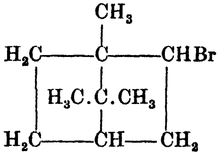
[†] *Ber.* 1872, **5**, 94, 628.

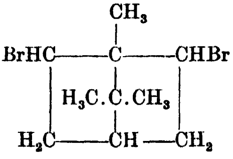
[‡] *Ibid.* 1872, **5**, 99, 215.

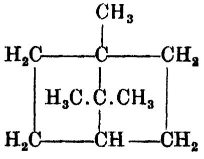
[§] *Ibid.* 1873, **6**, 437.

[‖] Flavitzky, *J. Russ. Phys. Chem. Soc.* 1889, **21**, 367; *J. pr. Chem.* 1892 [ii], **45**, 119; Tilden, *J.C.S.* 1888, **53**, 879; 1896, **69**, 1009; Stschukarev; *J. pr. Chem.* 1893 [ii], **47**, 191; Wallach, *Annalen*, 1891, **264**, 1; Armstrong, *J.C.S.* 1896, **69**, 1397.


(CLII)


(CLIII)


(CLIV)


(CLV)

Semmler to be incorrect,[†] since on reduction it gives *camphane* (CLV), whilst by the action of sodium it is converted into tricyclene. Semmler correctly identified it as bornyl dibromide. The remarks made above regarding the mechanism of the chlorination of α-pinene apply also to its bromination. The action of *N*-bromosuccinimide on α-pinene gives a *monobromo*-compound, b.p. 101–109°/12 mm.,[‡] which is probably identical with verbenyl bromide.[§]

---

[*] Compare Aschan, *Ber.* 1928, **61**, 43; Gallas and Montañés, *Anal. Fís. Quím.* 1930, **28**, 1163.

[†] *Ber.* 1900, **33**, 3423.

[‡] Ziegler, Späth, Schaaf, Schumann and Winkelmann, *Annalen*, 1942, **551**, 80.

[§] Buu-Hoï, Hiong-Ki-Wei, Lecomte and Royer, *Bull. Soc. chim.* 1946, p. 148.

Iodine reacts with α-pinene with great facility, but the products which are formed are very unstable, decomposing readily with formation of *p*-cymene.[*]

Although a complete and satisfactory explanation of the action of hydrogen chloride on α-pinene has only been given comparatively recently,[†] Kindt[‡] in 1802 made the historic observation that when hydrogen chloride was passed into oil of turpentine a crystalline substance separated, and to this he gave the name "artificial camphor". As was to be anticipated, this interesting substance, later known as "pinene hydrochloride", has been the subject of a large number of investigations,[§] and it was found that it could be prepared also by the passage of hydrogen chloride into solutions of oil of turpentine in various solvents such as carbon disulphide and benzene. It was further observed that the crystalline hydrochloride, the composition of which, $C_{10}H_{17}Cl$, was correctly determined by Dumas and by Blanchet and Sell, was always accompanied by liquid hydrochlorides of approximately the same composition. From this mixture Tilden succeeded in separating a crystalline dihydrochloride, $C_{10}H_{16}$, 2HCl, m.p. 50°, identical with that prepared from limonene, and he suggested that the liquid hydrochloride was probably a mixture of "artificial camphor" and dipentene dihydrochloride, which he showed experimentally to have a very low melting-point. This view was shared by Wallach,[‖] but the more recent experiments of Aschan,[¶] which are discussed on p. 172, have shown this to be not quite correct. For many years "artificial camphor" was naturally regarded as a true derivative of pinene, but the classical investigations of Berthelot,[**] supplemented by those of Riban,[††] rendered this improbable. Berthelot found that when hydrogen chloride was removed from "artificial camphor" pinene was not regenerated, but a new crystalline terpene, camphene, was formed. He concluded, therefore, that "artificial camphor" was a derivative of camphene, although it differed from the hydrochloride prepared by Riban by the action of hydrogen chloride on camphene. This latter hydrochloride is now known as *iso**bornyl chloride,* but the relationship of "artificial camphor" (*bornyl chloride*), *iso*bornyl chloride and camphene hydrochloride was only determined much later, and is discussed on p. 347. Berthelot's investigations, however, showed conclusively that "artificial camphor" was not a true derivative of pinene and paved the way for its subsequent recognition as bornyl chloride (CLVI).

---

[*] Deville, *Annalen*, 1841, **37**, 191; Kekule and Bruylants, *Ber.* 1873, **6**, 437; Oppenheim, *ibid.* 1874, **7**, 625; Preis and Rayman, *ibid.* 1879, **12**, 219; Armstrong, *ibid.* 1756; Denaro and Scarlato, *Gazzetta*, 1903, **33**, 393.

[†] Aschan, *Öfvers. Finska Vet. Soc.* 1914, **57**, no. 1; Meerwein and Emster, *Ber.* 1920, **53**, 1825; Meerwein and Emster, *ibid.* 1922, **55**, 2521.

[‡] *Tromms. J. Pharm.* 1802, **11**, II, 132.

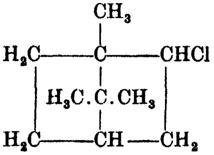
[§] *Inter al.*, Dumas, *Annalen*, 1832, **6**, 275; 1834, **9**, 56; Blanchet and Sell, *ibid.* 1832, **6**, 259; Berthelot, *Ann. Chim.* 1854 [iii], **40**, 5, 31; Tilden, *Ber.* 1879, **12**, 1131; Flavitzky, *J. Russ. Phys. Chem. Soc.* 1880, **12**, 57.

[‖] *Annalen*, 1887, **239**, 5.

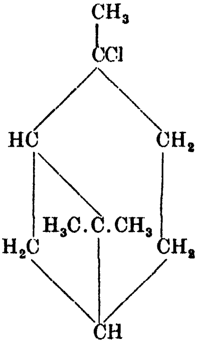
[¶] *Ibid.* 1912, **387**, 2.

[**] *Ibid.* 1859, **110**, 367; *Compt. rend.* 1862, **55**, 496.

[††] *Ann. Chim.* 1875 [v], **6**, 23, 363.



(CLVI)



(CLVII)

True *pinene hydrochloride* (CLVII) has been described by Aschan[*] and by Meerwein.[†] According to Aschan[‡] the hydrochloride is formed by the action of gaseous hydrogen chloride on α-pinene containing from 4 to 10 per cent. of ether at −15°, and is an oil having a suffocating odour. It was not obtained pure and free from bornyl chloride, but proof of its presence was deduced from the fact that on treatment of the crude hydrochloride with aniline the temperature rose to 80° and a mixture of bornyl chloride and α-pinene was obtained. The previous failure to prepare pinene hydrochloride Aschan ascribes to the fact that, at the ordinary temperature, the pinacolin change (p. 156) of pinene hydrochloride into bornyl chloride proceeds faster than the addition of hydrogen chloride to pinene. The experimental results described by Meerwein and his collaborators are not in complete agreement with those of Aschan. They found that when α-pinene in light petroleum solution was treated with hydrogen chloride at − 70° a crystalline pinene hydrochloride, mixed with bornyl chloride, was obtained. This chloride was immediately decomposed by either water or alcohol (hence the pungent smell noted by Aschan) and it titrated in these solvents like free hydrochloric acid. It was, however, stabilised by ether, although if this solvent was used as a diluent in its preparation, the velocity of the addition of hydrogen chloride was enormously decreased. In this fact they find a possible explanation of the isolation by Aschan of α-pinene by the action of aniline, which they suggest may have been present in his pinene hydrochloride owing to incomplete addition. It should be pointed out, however, that the marked rise in temperature which Aschan observed in this reaction does not support this explanation. The crystalline hydrochloride exhibits considerable stability, and it can be kept in ethereal solution at room temperature for several days without undergoing any change. The rate of conversion into bornyl chloride, in different solvents, increases in the following order: ether, light petroleum, toluene, chlorobenzene, anisole.

---

[*] *Öfvers. Finska Vet. Soc.* 1914, **57**, no. 11.

[†] Meerwein and Emster, *Ber.* 1922, **55**, 2521; Meerwein and Vorster, *J. pr. Chem.* 1936 [ii], **147**, 83.

[‡] A fuller account of these experiments is given by Aschan, *Naphtenverbindungen, Terpene und Campherarten*, pp. 191–197.

Aschan[*] and Kondakov and Saprikin[†] have attempted to prepare the hydrochloride indirectly by treating α-pinene with camphene hydrochloride or with the hydrochlorides of the bases, ammonia, hydroxylamine, trimethylamine, aniline, pyridine, cocaine and quinine. In all cases, however, isomerisation occurs with the formation of bornyl chloride.

By the action of hydrogen bromide and of hydrogen iodide on α-pinene, *bornyl bromide* and *bornyl iodide* are obtained, the corresponding true pinene derivatives not having been prepared.

Results of considerable interest have been obtained from a study of the action of hypochlorous acid on α-pinene, the earlier work on this subject by Wagner and his collaborators[‡] having been extended by Henderson and Marsh.* The reaction undoubtedly proceeds in a somewhat complicated manner and the interpretation of the results of Wagner and his collaborators is rendered difficult, since the method employed for the isolation of the products involved treatment with alkali and consequential secondary reactions. It is, however, clear that under the conditions used both by Wagner and by Henderson and Marsh one molecule of the hydrocarbon always reacts with two molecules of hypochlorous acid with fission of the *cyclo*butane ring. This being the case, it is obvious that the primary product of the reaction may be any one of the four *dichlorohydrins* (CLVIII), (CLIX), (CLX) and (CLXI), depending upon the direction in which the addition occurs. Apart from structural isomerism the possibility of both optical and *cis*-trans isomers has to be taken into account.

---

[*] *Öfvers. Finska Vet. Soc.* 1916, **58**, 1.

[†] *Bull. Soc. chim.* 1925 [iv], **37**, 726.

[‡] Wagner and Ginzberg, *Ber.* 1896, **29**, 886; Ginzberg, *J. Russ. Phys. Chem. Soc.* 1898, **30**, 686; Wagner and Slawinski, *Ber.* 1899, **32**, 2064.

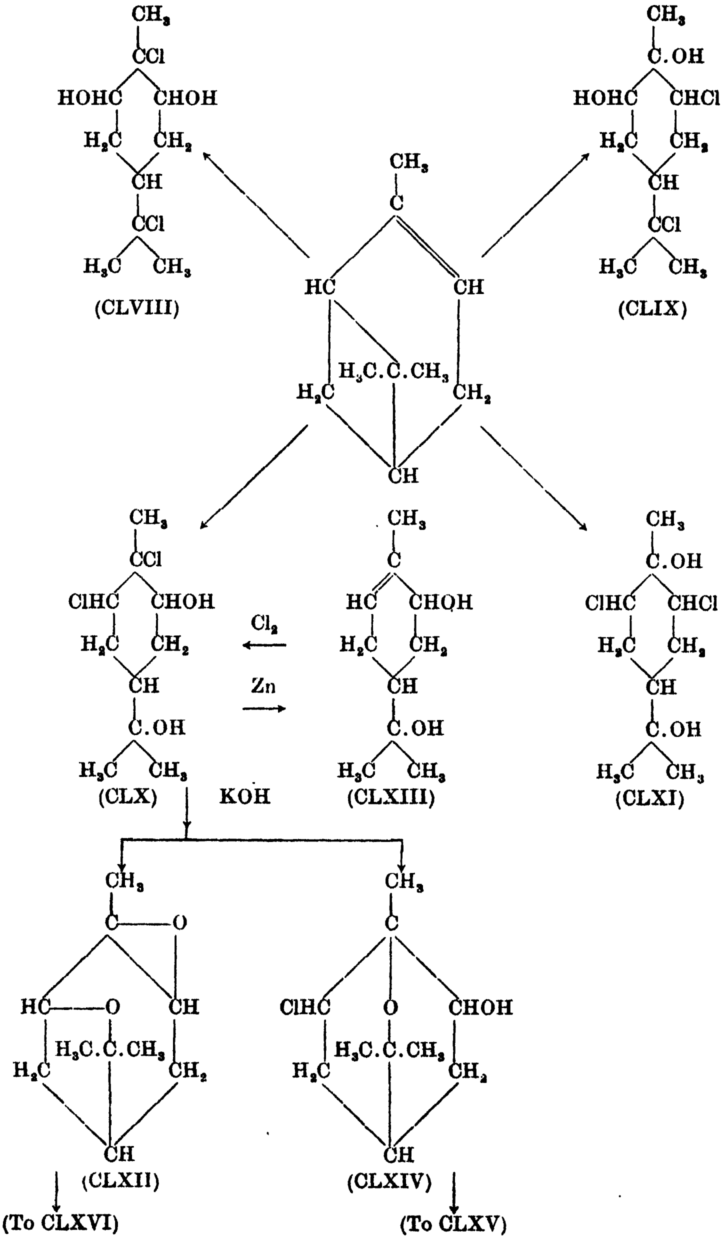
In their first experiments Wagner and Ginzberg treated α-pinene in ice-cold solution with hypochlorous acid and, after neutralisation of the excess of mineral acid with alkali, they obtained an optically inactive *monochlorohydrin*, $C_{10}H_{17}O_2Cl$, m.p. 105–107°, and an optically active isomeride, m.p. 131–133°, together with cis-*pinolglycol* (CLXVI). This result was confirmed by Ginsberg, who obtained in addition a dichloride, $C_{10}H_{16}Cl_2$, m.p. 165–168°, which was subsequently shown by Henderson and Marsh to melt at 176° and to be identical with bornyl dichloride.

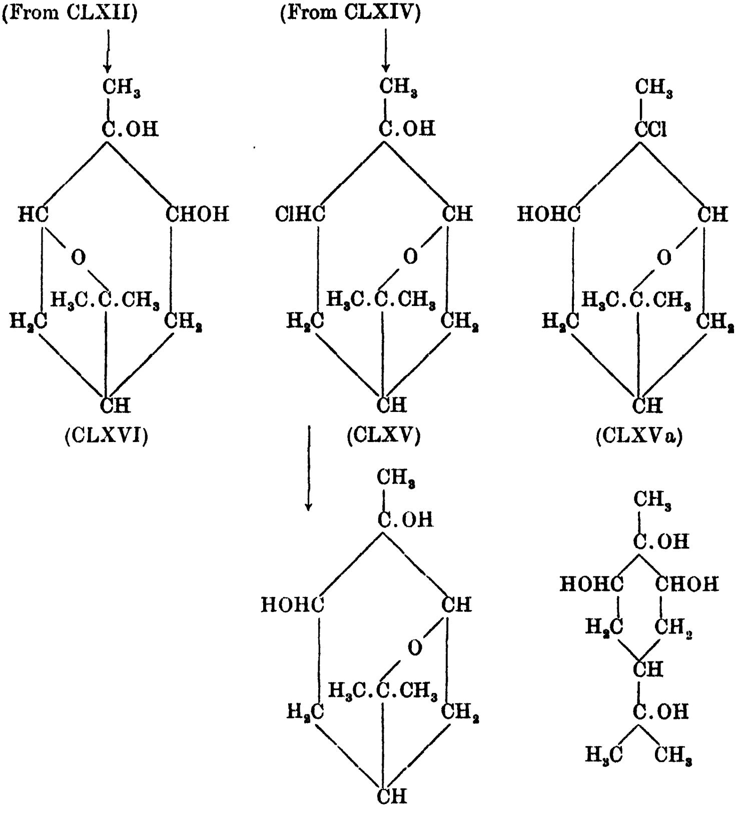
An insight into the mechanism of the formation of the monochlorohydrins resulted from the later work of Wagner and Slawinski. From the crude reaction mixture, which had the composition of a dichlorohydrin, $C_{10}H_{18}O_2Cl_2$, a crystalline solid slowly separated. This substance, which was optically active, melted at 136–137°, and was undoubtedly cis-1:2-*dichloro*-p-*menthane*-6:8-*diol* (*sobrerol dichloride*) (CLX), since, when treated with alkali, it gave *pinol oxide* (CLXII), whilst on reduction with zinc dust in alcoholic solution it gave sobrerol (CLXIII). This constitution for the dichlorohydrin was confirmed by Henderson and Marsh, who prepared it by the direct addition of chlorine to sobrerol.

As the greater part of the reaction product could not be obtained crystalline, Wagner and Slawinski resorted to treatment

---

* *J.C.S.* 1921, **119**, 1492.


(CLVIII)
(CLIX)
Cl₂
Zn
(CLX)
KOH
(CLXIII)
(CLXI)
(CLXII)
(To CLXVI)
(CLXIV)
(To CLXV)



(From CLXII)
(From CLXIV)

(CLXVI)
(CLXV)
(CLXVa)

(CLXVI)
(CLXVII)

with alkali in order to ascertain the nature of the substances present. They obtained in this manner (i) *pinol oxide* (CLXII), (ii) p-*menthane*-1:2:6:8-*tetrol* (*sobreroerythritol*) (CLXVII), m.p. 193–194°, (iii) an optically active *pinolglycolchlorohydrin*, m.p. 131–132° and (iv) in very small quantity, an isomeric pinolglycolchlorohydrin. The first two of these products can obviously result from any of the four possible dichlorohydrins, and therefore throw no light on the nature of the products present in the oil. The optically active pinolglycolchlorohydrin, m.p. 131–132°, α_D $+88{\cdot}3°$ and $-87{\cdot}39°$ (in the opposite sense to the α-pinene from which it was prepared), gave with alkali cis-*pinolglycol* (CLXVI), m.p. 123–124°. It must therefore have formula

(CLXV)[*] and should apparently result from the dichlorohydrin (CLXI). Whilst this is the simplest explanation of its formation, it can also be formed from the dichlorohydrin (CLX), since Henderson and Marsh found that when this substance was treated with very dilute alkali a *chlorohydrin*, m.p. 70–71°, was obtained, which readily gave a nitrobenzoate, m.p. 125°, and therefore contained a secondary alcohol group. This glycol, to which they gave formula (CLXIV), passed with extreme facility into the optically inactive form of (CLXV), m.p. 104°, which was also prepared by mixing equal quantities of the *d*- and *l*-forms, m.p. 131–132°. From the experiments of Wagner and his collaborators, therefore, the conclusion may be drawn that by the action of hypochlorous acid on α-pinene the main product formed is the dichlorohydrin (CLX) with possibly a small quantity of (CLXI). Henderson and Marsh were, however, successful in separating two more crystalline dichlorohydrins; one of these, m.p. 124–126°, was optically active and must be 2 : 8-*dichloro*-p-*menthane*-1 : 6-*diol* (CLIX), since this formula alone of the remaining formulae allows of optical activity. On treatment with alkali it gave *l*-pinolglycol-2-chlorohydrin (CLXV) with a trace of pinol oxide. The other dichlorohydrin, m.p. 155°, was also optically active; Henderson and Marsh suggested that it is derived from β-pinene, but the quantity available was insufficient for an investigation of its reactions.

As mentioned above, Ginzberg obtained bornyl dichloride by the action of hypochlorous acid on α-pinene, and the corresponding bromide appears to be the main product when hypobromous acid is used.[†] The mechanism involved in the formation of the dihalide derivatives has not been determined. They can result either from the presence of free halogen in the acid used, or by the elimination of water from an intermediate product of the type (CLXVIII).

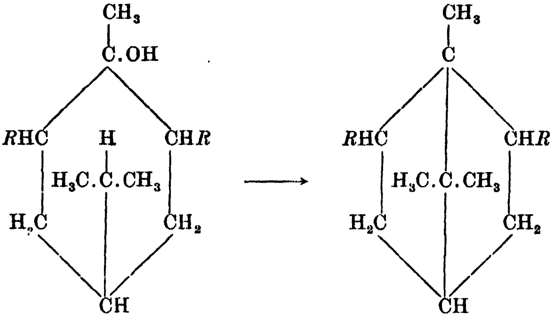
By the action of the phosphorus halides, thionyl chloride and analogous reagents, either *p*-cymene or the bornyl halides result. Thus with phosphorus trichloride Naudin[‡] obtained *p*-cymene in

---

[*] The alternative formula (CLXVa) cannot be correct, since this substance, m.p. 52–54°, was prepared by Ginzberg (*J. Russ. Phys. Chem. Soc.* 1908, **30**, 681) by the action of hypochlorous acid on pinol and was found to contain a secondary alcohol group.

[†] Wagner and Ginzberg, *Ber.* 1896, **29**, 890.

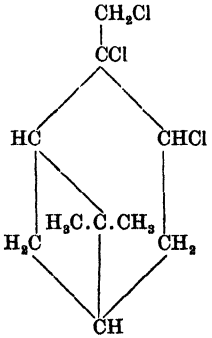
[‡] *Bull. Soc. chim.* 1882 [ii], **37**, 111.



(CLXVIII)

R = Cl or Br

a yield of 75 per cent., whilst with the pentachloride at 25° Bert* obtained a mixture of *p*-cymene (13 per cent.), a diterpene and a mixture of chlorides, one of which, $C_{10}H_{16}Cl_2$, m.p. 183°, was probably bornyl dichloride. Schmidt† claimed that thionyl chloride and sulphuryl chloride react with α-pinene to give bornyl chloride in a yield of 80 per cent., but the experiments of Garino and D'Ambrosio‡ showed that at least in the case of the former reagent the reaction is very much more complex. From α-pinene they prepared a liquid dichloride, $C_{10}H_{16}Cl_2$, which they regarded as a true pinene derivative, and which on distillation in steam decomposed, yielding a mixture of bornyl chloride and a *trichloride* which they represented by (CLXIX). In view, however, of the known instability of the halogenated pinanes, it seems very unlikely that the substance can have this formula, and until



(CLXIX)

---

* *Bull. Soc. chim.* 1923 [iv], **33**, 787.

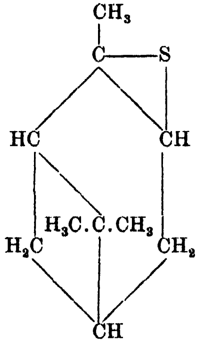
† *G.P.* **397314.**

‡ *Gazzetta,* **1924, 54, 345.**

direct evidence of the presence of the *cyclo*butane ring is forthcoming, it is probably best regarded as a trichlorocamphane or fenchane.

Aluminium chloride polymerises α-pinene to a crystalline substance, $(C_{10}H_{16})_n$, m.p. 77–78°, which when heated with the reagent is depolymerised to substances resembling in their properties the so-called naphthenes.[*]

In view of Ruzicka's successful application of Atterberg's method of dehydrogenation with sulphur to the elucidation of the structure of the sesquiterpenes, it is of interest to note that Budnikov and Schilov[†] have found that α-pinene reacts with sulphur to give an additive-derivative which, from analogy with the ozonide, is given formula (CLXX). Although the compound itself could not be purified, it gave a crystalline *methoiodide*, m.p. 121°.



(CLXX)

Reference has been made already to the important derivative *pinene nitrosochloride*, and the constitution and reactions of this substance must now be discussed. Pinene nitrosochloride was first prepared by Tilden[‡] by the action of nitrosyl chloride on the hydrocarbon, and its properties were subsequently studied by him in collaboration with Shenstone.[§] Some years later Wallach[||] simplified the preparation by substituting for nitrosyl chloride a mixture of amyl nitrite (or ethyl nitrite) and hydrochloric acid;

---

[*] Steinkopf and Freund, *Ber.* 1914, **47**, 411.

[†] *Ber.* 1922, **55**, 3848; compare Nakatsuchi, *J.S.C.I. Japan*, 1930, **33**, 408 B.

[‡] *J.C.S.* 1875, **28**, 514.

[§] *Ibid.* 1877, **31**, 554.

[||] *Annalen*, 1888, **245**, 201; 1889, **253**, 251.

whilst this method is now in general use, the yield of nitrosochloride is considerably smaller than that obtained by Tilden's original method.* Pinene nitrosochloride can be purified by recrystallisation from either benzene or chloroform, but it is decomposed if heated for any length of time with either of these solvents. The melting-point as originally determined by Tilden and Shenstone was 103°, but according to Tilden this is too low. When well washed with alcohol and dried it melts at 109–111° and after recrystallisation from chloroform at 115°. Since the melting is accompanied by decomposition, it varies somewhat with the rate of heating and is, as a general rule, found to be about 105–108°.

In his early investigation it was observed by Tilden that the same pinene nitrosochloride, which was optically inactive, was obtained independent of whether *d*- or *l*-α-pinene was used in its preparation, and, further, that the yield of nitrosochloride diminished with increase of the rotatory power of the terpene. The cause of this apparent anomaly has been found by Lynn† to lie in the much greater solubility and instability of the optically active nitrosochlorides. By suitable modification of the experimental conditions Lynn has prepared the two optically active nitrosochlorides, m.p. 81–81·5°, $[\alpha]_D$ ±322°.

In the absence of molecular weight determinations pinene nitrosochloride was given the simple formula $C_{10}H_{16}ONCl$, and was represented as an oximino chloride (CLXXI).‡ Although this formula is in full accord with its reactions, it has been shown that, as originally suggested by Baeyer,§ the colourless crystalline solid is bimolecular (CLXXII).

The reactions of pinene nitrosochloride have been very thoroughly investigated and it has been found to yield products of great interest, many of which have been of fundamental importance in the development of terpene chemistry. In view of the somewhat indefinite melting-point of the nitrosochloride, Wallach's observation,‖ that it gave on treatment with organic

---

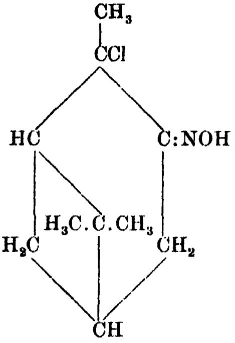
* Cf. Tilden, *J.C.S.* 1904, **85**, 760.

† *J. Amer. C.S.* 1919, **41**, 361; compare Thurber and Thielke, *ibid.* 1931, **53**, 1030.

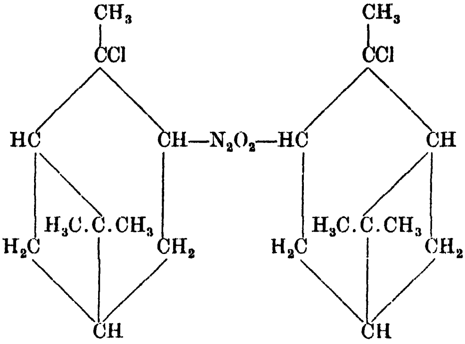
‡ The constitution of pinene had of course not been determined at the time of Tilden's original experiments.

§ *Ber.* 1895, **28**, 648.

‖ *Inter al.*, *Annalen*, 1888, **245**, 253; 1889, **252**, 130; 1892, **268**, 216.



(CLXXI)



(CLXXII)

bases highly crystalline *nitrolamines*, was of great value. With benzylamine the *nitrolbenzylamine*, m.p. 122–123°, and with piperidine the *nitrolpiperidide*, m.p. 118–119°, can be prepared, the corresponding optically active modifications melting according to Lynn at 144–145° and 84° respectively. Leach[*] has prepared the simplest *pinene nitrolamine*, m.p. 137°, by treatment of the nitrosochloride with ammonia. When the nitrosochloride is treated with aniline under the usual conditions, however, contrary to expectation Wallach[†] found that the parent hydrocarbon was regenerated. This abnormal and apparently unique reaction provided a valuable method for the preparation of pure *dl*-α-pinene free from β-pinene, and, as mentioned on p. 118, enabled Baeyer to prove that nopinic acid was derived from the latter hydrocarbon. More recently Lynn by the use of this reaction has prepared *d*- and *l*-α-pinenes from the optically active nitrosochlorides. In an attempt to find an explanation for this abnormality, the reaction has been studied in some detail by Earl and Kenner,[‡] who have shown that, if the nitrosochloride is allowed to react with aniline in alcoholic solution in the presence of sodium acetate, *pinene nitrolanilide*, m.p. 122°, can be prepared. They consider the formation of the hydrocarbon to be due to the great tendency for elimination of hydrogen chloride to occur with formation of *nitrosopinene* and they offer a theoretical explanation to account for this.

---

[*] *J.C.S.* 1907, **91**, 1.

[†] *Annalen*, 1889, **252**, 132; 1890, **258**, 343.

[‡] *J.C.S.* 1927, p. 1269.

The instability of pinene nitrosochloride and the facility with which it could be converted into *nitrosopinene* was observed by Tilden, who showed that this substance, which had the composition $C_{10}H_{15}ON$, m.p. 132°, could be readily prepared by the action of an alcoholic solution of potassium hydroxide on the nitrosochloride. Wallach and Lorentz[*] found sodium ethoxide to be a more convenient reagent, whilst Earl and Kenner observed that it was formed when the nitrosochloride was boiled with carbon tetrachloride. The constitution of nitrosopinene has been the subject of considerable controversy and it is only recently that definite proof of its structure has been obtained. Tilden considered it to be a true nitroso derivative and this view was, for a time, shared by Wallach,[†] although Goldschmidt and Zürrer[‡] had pointed out that, since it was soluble in both acids and alkalis, it contained most probably an iso*nitroso* group, confirmation of which was obtained by the preparation of a sodium derivative and a methyl ether. Further experimental evidence in favour of the *iso*nitroso constitution was provided by the experiments of Urban and Kremers[§] and of Kremers,[‖] who showed that on digestion with acids a mixture of hydroxylamine and carvacrol was obtained. This reaction evidently proceeded with the intermediate formation of *carvoxime hydrochloride*, which Baeyer[¶] found was formed when nitrosopinene was treated in the cold with hydrogen chloride. The presence of an *iso*nitroso group being thus established, the most obvious constitution was that represented by (CLXXIII), simple elimination of hydrogen chloride from the nitrosochloride having occurred. This view of the mechanism of the reaction received support from the experiments of Deussen.[**] He showed that nitrosopinene gave a *phenylurethane*, m.p. 101–102°, and that, when the nitrosochloride was treated with sodium methoxide, in addition to nitrosopinene, a *methyl ether*, $C_{11}H_{19}O_2N$ (CLXXIV), m.p. 101–102°, was obtained. This substance, like nitrosopinene, must contain an *iso*nitroso group, since it gives a *phenylurethane*, m.p. 102°, and on treatment with hydrogen chloride gives dl-*carvoxime hydrochloride* (CLXXV).

---

[*] *Annalen*, 1892, **268**, 198; compare Vitte, *Bull. Inst. Pin*, 1933, p. 216.

[†] *Ber.* 1891, **24**, 1547; 1895, **28**, 1313.

[‡] *Ibid.* 1885, **18**, 2223.

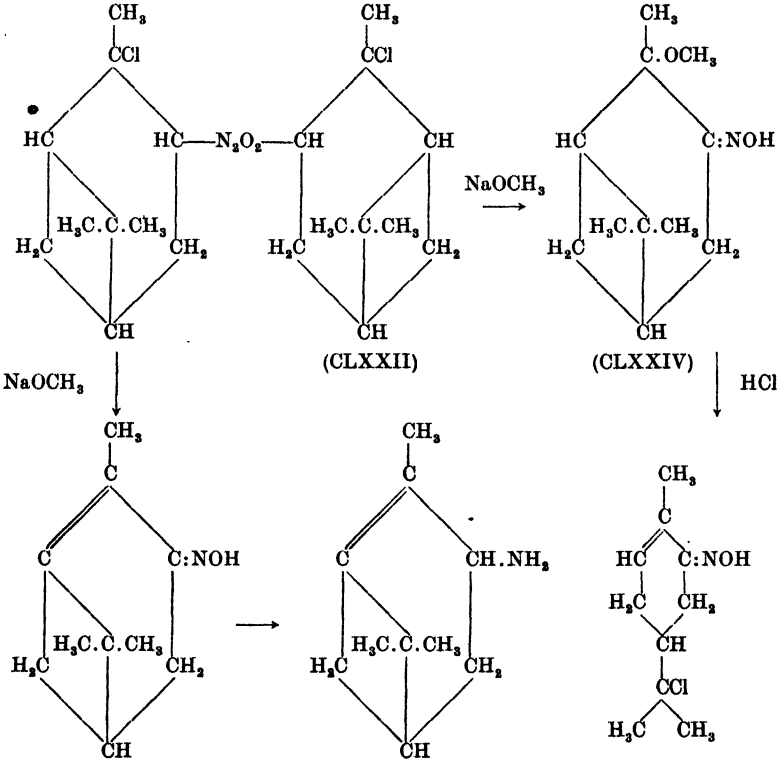
[§] *Amer. Chem. J.* 1894, **16**, 404.

[‖] *Ibid.* 1895, **17**, 607.

[¶] *Ber.* 1896, **29**, 12.

[**] *Annalen*, 1910, **374**, 110.

According to Deussen these reactions may be formulated:



(CLXXII) (CLXXIV) (CLXXIII) (CLXXVI) (CLXXV)

Although this formula for nitrosopinene was generally accepted,[*] it formed a notable exception to Bredt's rule,[†] that substances having an ethylenic linkage attached to the bridgehead of the dicyclic system were extremely unstable and tended to isomerise to a more stable form. Now nitrosopinene is a substance of very considerable stability. It can be reduced by zinc dust and acetic acid to the corresponding unsaturated amine, *pinylamine*,[‡] b.p. 90°/12 mm., $d^{20°}$ 0·9440, $n_D^{20°}$ 1·5036, which, accepting the formula (CLXXIII) for nitrosopinene, must be

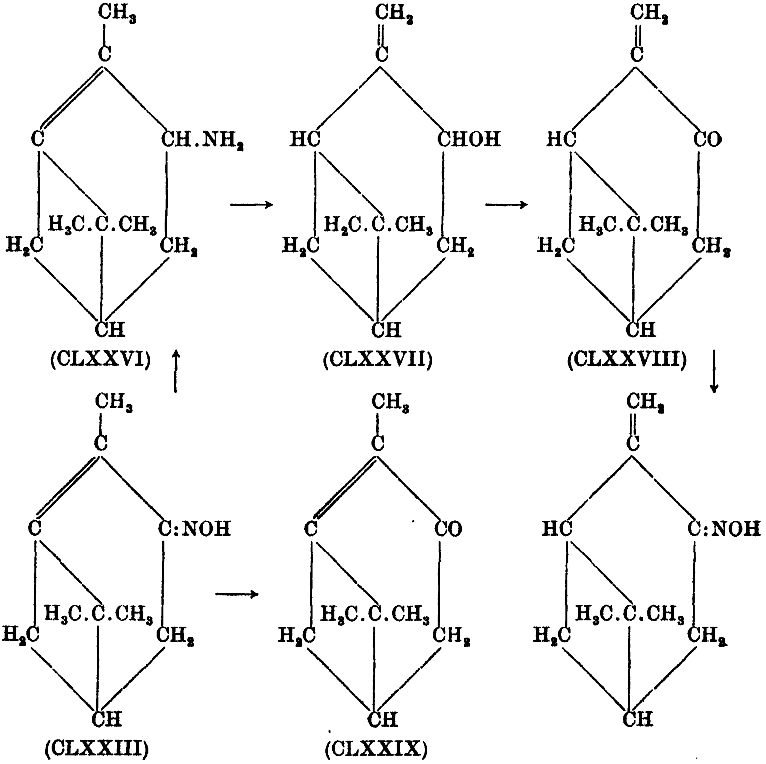
---

[*] Compare Wallach, *Annalen*, 1912, **389**, 185.

[†] *Ber.* 1902, **35**, 1286; *J. pr. Chem.* 1917 [ii], **95**, 132.

[‡] Wallach, *Annalen*, 1890, **258**, 346; 1892, **268**, 197; 1898, **300**, 287; 1906, **346**, 240.

(CLXXVI). Like nitrosopinene, pinylamine is a stable substance, which is not in agreement with this formula. Wallach[*] had shown that pinylamine on treatment with nitrous acid gave a secondary alcohol, thought to be pure *pinocarveol* (CLXXVII), from which by oxidation a product assumed to be *pinocarvone* (CLXXVIII) was prepared. The *oxime* from this melted at 98° and was not identical with nitrosopinene; furthermore, on reduction it gave an amine, pinocarvylamine, different from pinylamine. Wallach's view that nitrosopinene and pinocarvoxime had different structures appeared to receive support from his further observation[†] that when nitrosopinene was warmed with oxalic acid it gave a ketone, *carvopinone*, which reacted with hydroxylamine to yield nitrosopinene; it also gave a semicarbazone which melted above



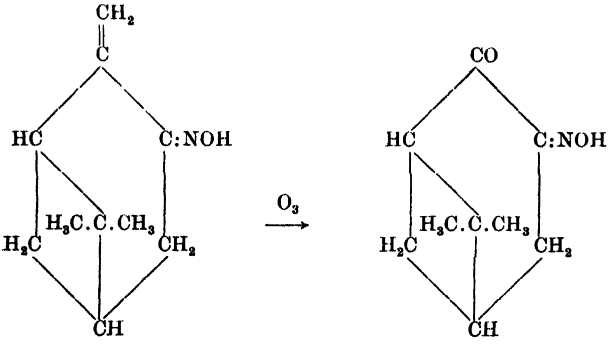
---

[*] *Annalen*, 1906, **346**, 221.

[†] *Ibid.* p. 231.

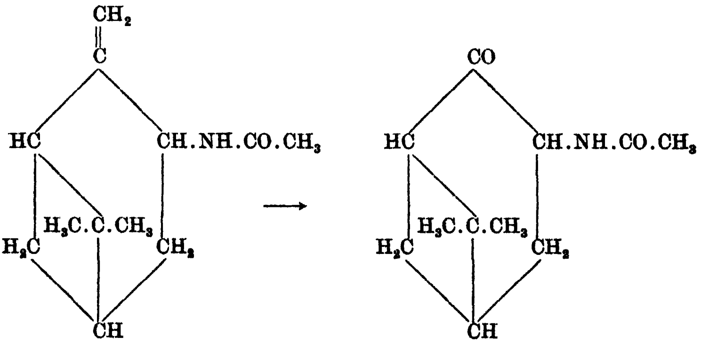
300° and was thus different from pinocarvone semicarbazone, m.p. 204°. Carvopinone was formulated as (CLXXIX). These substances all contained the *cyclo*butane ring, since on oxidation they gave pinic acid, and to account for their formation Wallach represented the changes occurring in accordance with the scheme shown on p. 183.

The problem was reinvestigated by Ruzicka and Trebler* who found that when nitrosopinene is oxidised with ozone it yields iso*nitrosonopinone* (CLXXX), whilst acetylpinylamine gives with the same reagent *acetyl*-1-*aminonopinone* (CLXXXI). These experiments prove conclusively that nitrosopinene and acetylpinylamine must be derivatives of β-pinene and have formulae (CLXXXII) and (CLXXXIII) respectively.



(CLXXXII)

(CLXXX)



(CLXXXIII)

(CLXXXI)

---

* *Helv. Chim. Acta*, 1921, **4**, 566.

In order to explain the results obtained by Wallach it was suggested by Ruzicka and Trebler that nitrosopinene and pinocarvoxime, pinylamine and pinocarvylamine were stereo-isomerides and not structural isomerides. They retained formula (CLXXIX) for carvopinone, since it had only been obtained from nitrosopinene in very small yield, and when its semicarbazone was hydrolysed with oxalic acid isomerisation occurred to a considerable extent with the formation of carvone.

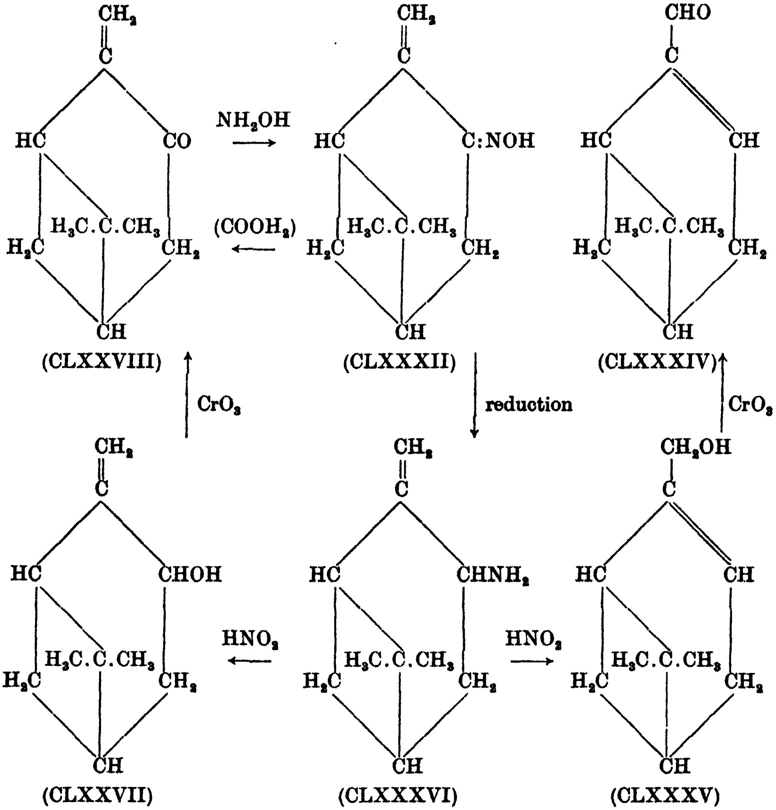
Recently, however, it has been shown by Schmidt[*] that certain inaccuracies in the experimental results outlined above have led to a somewhat remarkable series of errors. It is now clear, from evidence which is discussed more fully on p. 224, that the substance which has hitherto been described as pinocarvone is in reality *myrtenal* (CLXXXIV) and it is therefore not surprising that the oxime, m.p. 98°, now recognised to be myrtenal oxime, is not identical with nitrosopinene. As already mentioned, the latter substance was found by Wallach to be identical with the oxime of carvopinone, and this is explained by the fact that "carvopinone" is actually the true pinocarvone (CLXXVIII). The action of nitrous acid on pinylamine (CLXXXVI) does not give pure pinocarveol (CLXXVII) but a mixture of alcohols, and it is ironic that Wallach was probably correct in his conclusion that the product was identical with his natural pinocarveol, since it is now known that pinocarveol is accompanied in *Eucalyptus globulus* by *myrtenol* (CLXXXV). The oxidation product would therefore contain both pinocarvone and myrtenal, and it is interesting to note that although Wallach isolated only one oxime, m.p. 98°, he obtained two semicarbazones, one melting at 209°, and the other above 300°; furthermore, he suggested that the second was probably the same as "carvopinone" semicarbazone, but the significance of this observation was apparently not realised. The first semicarbazone is, of course, that of myrtenal, whilst the high melting isomer is a true derivative of pinocarvone. The relationships of the compounds concerned may, therefore, be summarised in the scheme shown on p. 186.

A number of interesting derivatives of pinene nitrosochloride have been prepared. Forster and Newman[†] showed that when

---

[*] *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530.

[†] *J.C.S.* 1911, **99**, 244.

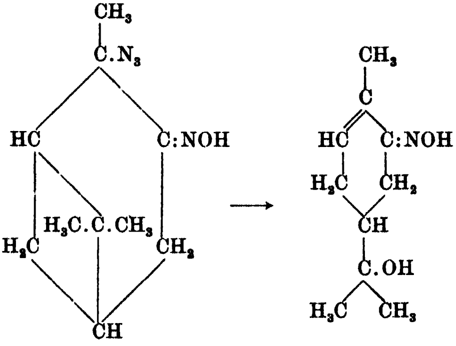


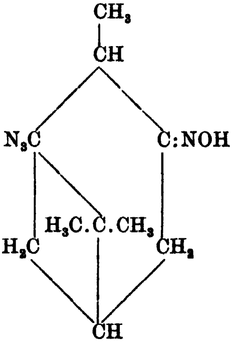
it is treated with sodium azide it yields *pinene nitrosoazide*, $C_{10}H_{16}ON_4$ (CLXXXVII), m.p. 120°. By the action of sodium ethoxide the azide is converted into nitrosopinene, whilst on digestion with water it gives a mixture of *hydroxydihydrocarvoxime* (CLXXXVIII) and an isomeric pinene nitrosoazide, m.p. 126°, which Forster and Newman considered to be the structural isomeride (CLXXXIX), since it also gives nitrosopinene when treated with sodium ethoxide. This constitution would, however, appear unlikely and the two isomerides are much more probably stereoisomerides.

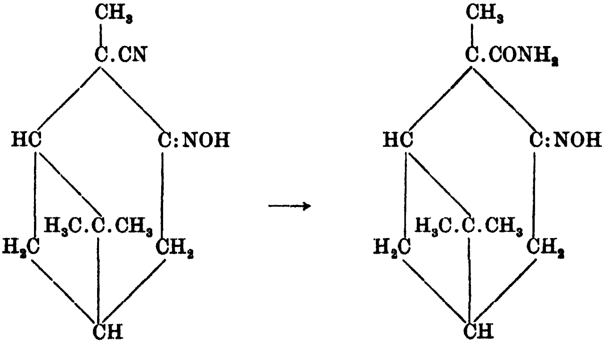
By the action of potassium cyanide on pinene nitrosochloride Tilden and Burrows* prepared a *nitrile*, $C_{11}H_{16}ON_2$, m.p. 171°, which doubtless has formula (CXC), simple replacement of the halogen atom by the cyano group having occurred. The nitrile is readily soluble in alkali and may be characterised by the preparation of the *methyl ether*, m.p. 67°, and the *benzoyl* derivative, m.p. 102°. The cyano group is very resistant to hydrolytic agents, but with concentrated sulphuric acid it yields an *amide*, m.p. 220°, which in the absence of any isomeric change must have formula (CXCI). The corresponding acid could not be prepared, further hydrolysis being accompanied by ring fission; the nature of the products has only been incompletely investigated and their constitution has not been determined.

---

* *J.C.S.* 1905, **87**, 344; compare Tilden and Blyther, *ibid.* 1906, **89**, 1563.


(CLXXXVII) (CLXXXVIII)

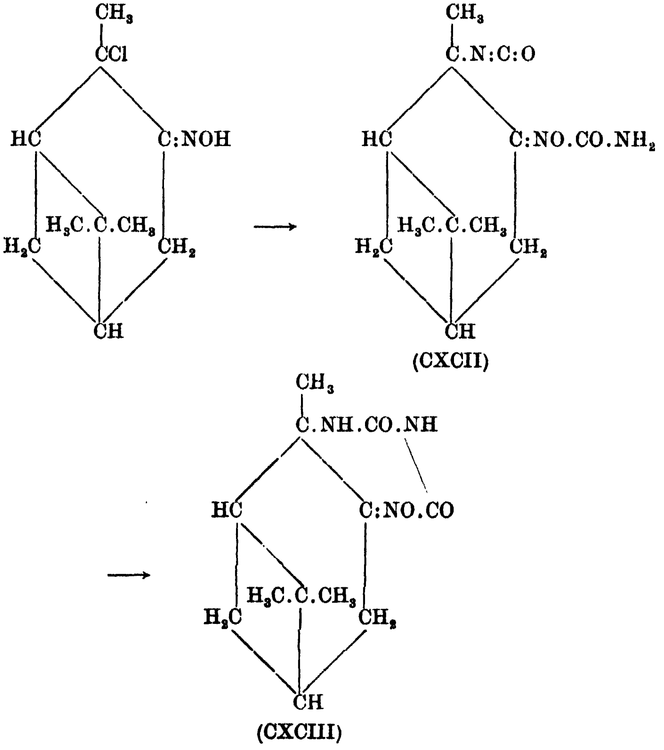

(CLXXXIX)


(CXC) (CXCI)

Leach* found that with potassium cyanate pinene nitrosochloride reacts in a somewhat different manner, two molecules of the cyanate reacting with one of the nitrosochloride to give an *imide* (CXCIII), m.p. 238–240°. This imide results probably from the combined action of free cyanic acid and potassium cyanate on the nitrosochloride, the intermediate product (CXCII) being first formed. The imide is remarkably stable to oxidising agents, but with concentrated sulphuric acid it yields pinene nitrolamine, and with alkali nitrosopinene.

---

* *J.C.S.* 1907, 71, 10.



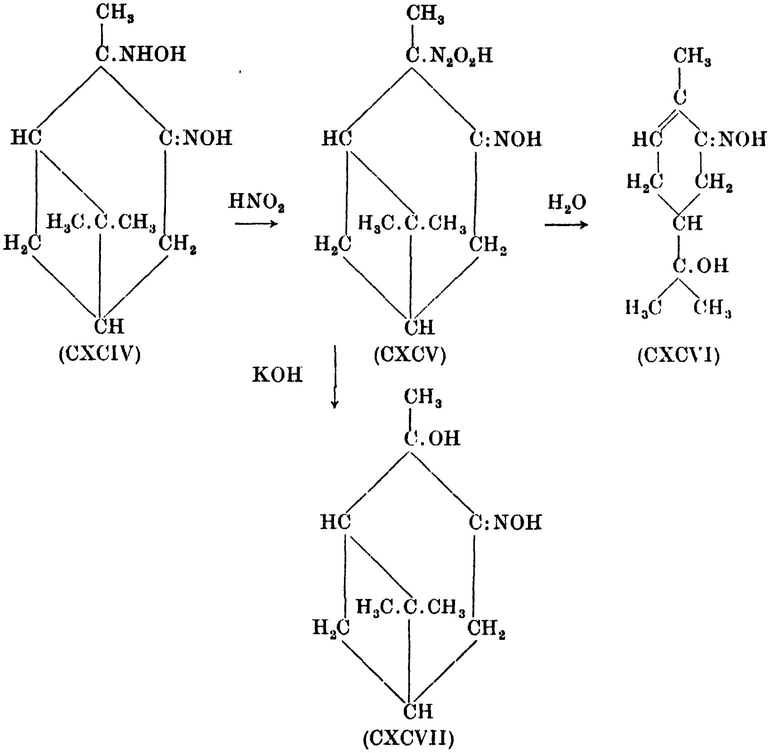
(CXCII)

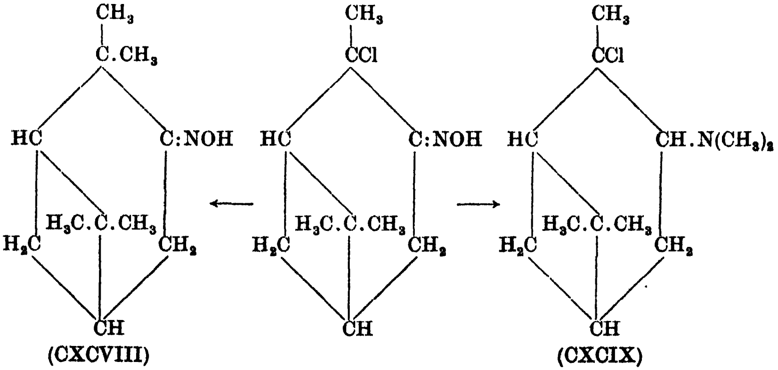
(CXCIII)

Cusmano[*] studied the action of hydroxylamine on pinene nitrosochloride and found it to yield *pinene hydroxylamino-oxime* (CXCIV), m.p. 140°. This interesting substance gives with nitrous acid the iso*nitroamino-oxime* (CXCV), m.p. 127°, which, when warmed with water or dilute acetic acid, is converted into *hydroxydihydrocarvoxime* (CXCVI), and with alkali into a mixture of *hydroxypinocamphoneoxime* (CXCVII), m.p. 128°, and nitrosopinene. It undergoes coupling reaction with diazonium salts.*

---

[*] *Gazzetta*, 1910, **40**, ii, 122.





---

* d'Ambrosio, *Gazzetta*, 1932, **62**, 271.

Finally, mention must be made of the experiments of Tilden and Stokes* on the action of methyl magnesium iodide on the nitrosochloride. This reagent is found to react with both the halogen atom and the *iso*nitroso group, yielding *methylpinocamphoneoxime* (CXCVIII), m.p. 193°, and *chlorodihydrodimethylpinylamine* (CXCIX), m.p. 122°.

With maleic anhydride, α-pinene slowly forms an *adduct*, of which the free dibasic acid has m.p. 169°. With maleic acid, however, a vigorous reaction occurs, to give the adduct of α-terpinene (Vol. I, p. 186).

Lextreit† made the somewhat remarkable observation that pinene combined with picric acid to yield a crystalline derivative, m.p. 133°, which was decomposed by alkali yielding borneol. This compound was investigated subsequently by Tilden and Forster,‡ who showed that when it was heated above its melting-point it decomposed with the formation of camphene, a reaction which occurred also when its solution in pyridine was distilled. These reactions leave no doubt that "pinene picrate" is not a derivative of α-pinene, and this has been confirmed by the more recent experiments of Delépine and Adida,§ who have shown that by the interaction of the optically active forms of α-pinene with picric acid in benzene solution at 120° it is possible to prepare d-*bornyl picrate*, m.p. 134°, $[\alpha]_D$ +78°, and d-*fenchyl picrate*, m.p. 106°, $[\alpha]_D$ +22° (or their optical enantiomorphs), which can be separated by fractional crystallisation.

According to Alder and Stein‖ α-pinene reacts with phenylazide to give a compound $C_{16}H_{21}N_3$, m.p. 77°. An addition compound of α-pinene and hydroferrocyanic acid has been described by Stephan and Hammerich.¶

Owing to its tendency to isomerise α-pinene has not been used in many synthetical investigations, and reference need only be made to the experiments of Buchner and Rehorst,** in which they condensed the hydrocarbon with ethyl diazoacetate and prepared the *tricyclic* ester (CC), b.p. 135°/12·5 mm., $d_{4°}^{16°}$ 1·0059,

---

* *J.C.S.* 1905, **87**, 836.

† *Compt. rend.* 1886, **102**, 555.

‡ *J.C.S.* 1893, **63**, 1388; compare Murayama and Otsuka, *J. Pharm. Japan*, 1924, **513**, 909.

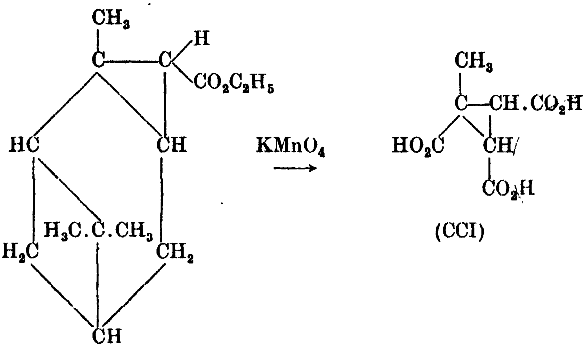
§ *Bull. Soc. chim.* 1926 [iv], **39**, 782.

‖ *Annalen*, 1935, **515**, 175.

¶ *J. pr. Chem.* 1931 [ii], **129**, 285.

** *Ber.* 1913, **46**, 2680.

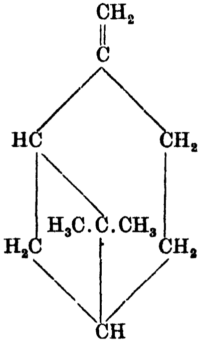
n_D 1·4828, which gave on hydrolysis the corresponding acid, m.p. 165°. Oxidation of this acid with potassium permanganate gave terebic acid and *methyl*cyclo*propane*-1:2:3-*tricarboxylic acid* (CCI), m.p. 192°.



(CC)

(CCI)

β-PINENE (NOPINENE)



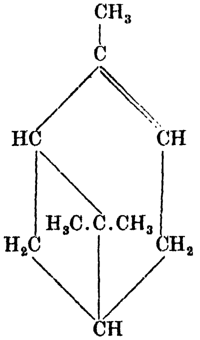
l-*β*-Pinene occurs in nature in the majority of the oils in which *α*-pinene is found; the percentage present however is very variable, and is, as a rule, considerably lower than that of the latter. The dextrorotatory hydrocarbon has apparently only been separated from two oils, Rutovski and Vinogradova* having established its presence in the oil from the ripe fruits of *Ferula galbaniflua*, and Nelson† having obtained it from the volatile oil of *Cynomarathrum nuttallii*; in every other case the natural hydrocarbon has been found to be laevorotatory.

---

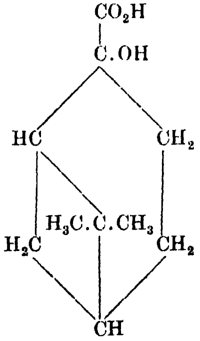
* *J. pr. Chem.* **1928** [ii], **120, 44.**

† *J. Amer. C.S.* **1933, 55, 3400.**

Since β-pinene does not yield any crystalline derivatives and can only be separated from α-pinene by prolonged fractional distillation, it is not surprising that its discovery was fortuitous. During his investigation of the products formed by the oxidation of French oil of turpentine with potassium permanganate, Baeyer[*] obtained in small quantity an acid which gave a sparingly soluble sodium salt. This acid, *nopinic acid*, $C_{10}H_{16}O_3$, m.p. 126–127°, $[\alpha]_D$ − 16·28° (in ether), was not formed when pure α-pinene (from the nitrosochloride) was oxidised under similar conditions, and Baeyer naturally suggested that it originated from another hydrocarbon. Shortly afterwards, from a study of its reactions, Baeyer and Villiger[†] correctly deduced that it must be represented by formula (II), but they concluded, incorrectly, that it was formed from α-pinene (I) by simultaneous oxidation of the methyl group with addition of water to the ethylenic linkage.



(I)



(II)

Nopinic acid was isolated also by Tiemann and Semmler[‡] and by Wagner and Ertschikowski.[§]

Baeyer and Villiger based their formula for nopinic acid on the following evidence. When the acid was oxidised with lead peroxide it gave a ketone, nopinone, $C_9H_{14}O$, and it was therefore an α-hydroxy acid. Nopinone was a saturated ketone and gave on oxidation with nitric acid *homoterpenylic* acid (IV), a reaction which was explained most simply if nopinone was the dicyclic ketone (III).

---

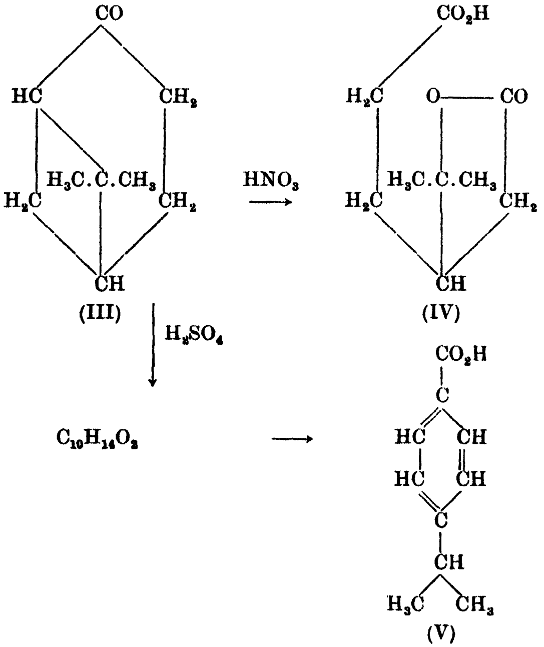
[*] *Ber.* 1896, **29**, 25.

[†] *Ibid.* p. 1923.

[‡] *Ibid.* p. 532.

[§] *Ibid.* p. 881.

On digestion with dilute sulphuric acid nopinic acid gives by fission of the *cyclo*butane ring an acid, $C_{10}H_{14}O_2$, m.p. 130–133°, which must be a *dihydrocumic acid*, since on oxidation with potassium ferricyanide *cumic acid* (V) is obtained. The constitution of the dihydro-acid has not been determined, but one of the ethylenic linkages is probably in the Δ^1-position. Ring fission also occurs when nopinic acid is treated with hydrogen bromide in acetic acid solution, a *bromotetrahydrocumic acid*, $C_{10}H_{15}O_2Br$, m.p. 175°, being obtained. The constitution of this acid has also not been determined, but treatment with silver acetate results in the formation of a second *dihydrocumic acid*, m.p. 125°, from which cumic acid can be prepared by oxidation with potassium ferricyanide. These experiments, yielding as they did cumic acid and homoterpenylic acid, showed that the *iso*propyl group must form part of the ring structure in nopinic acid and nopinone, and



supported therefore the formulae suggested by Baeyer and Villiger. Although subsequent investigations have shown that these formulae are correct, the further assumption, that the hydroxy acid was derived from α-pinene, has been shown to be erroneous. Wagner and Slawinski[*] were apparently the first to point out that the acid was more probably derived from an isomeric hydrocarbon containing an exocyclic ethylenic linkage. This hydrocarbon, to which the name β-pinene or nopinene was given, was not however obtained pure until many years later, but confirmatory evidence of its existence was furnished by the observation that nopinic acid, whether prepared from dextro- or laevorotatory oil of turpentine, was always laevorotatory. Although nopinone was first characterised by Baeyer and Villiger, who prepared the *semicarbazone*, m.p. 188°, it had actually been isolated previously from the neutral oxidation products of oil of turpentine which were volatile in steam.[†] The further investigation of the reactions of this ketone has been due mainly to Wallach. He found that it could be prepared much more conveniently from nopinic acid, if an acid solution of potassium permanganate was used in place of lead peroxide.[‡] The ketone, which melts somewhat above 0°, has the following constants:[§] b.p. 209°, $d^{20°}$ 0·981, $n_D^{20\cdot5°}$ 1·4787, $[\alpha]_D$ + 18·48°, yields a *monobenzylidene* derivative, m.p. 106–107°,[‖] but, if hydrogen chloride is used as the condensing agent, a *chlorodibenzylidene* derivative, m.p. 148–149°, is obtained, which has the structure (VI).[¶]

When nopinone is treated with hydrogen chloride in alcoholic solution, ring fission, together with condensation, occurs with the formation of a bimolecular *trichloride*, $C_{18}H_{29}OCl_3$, m.p. 148°, to which Wallach and Blumann[**] assign formula (VII). This trichloride is very sparingly soluble and is well suited for the characterisation of the ketone. On treatment with sodium methoxide the trichloride loses hydrogen chloride, yielding a *dichloride*, $C_{18}H_{28}OCl_2$, m.p. 125–126°, which is reconverted by hydrogen chloride into the trichloride. The tendency for nopinone to yield monocyclic derivatives is shown further by its conversion

[*] *Ber.* 1899, **32**, 2082.

[†] Compare Wallach, *Annalen*, 1900, **313**, 363.

[‡] *Annalen*, 1907, **356**, 231.

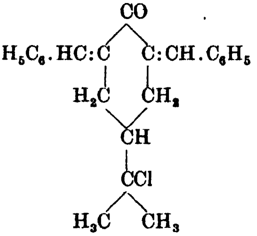
[§] Compare Östling, *J.C.S.* 1912, **101**, 474.

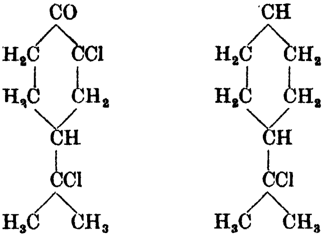
[‖] Wallach, *Annalen*, 1900, **313**, 363.

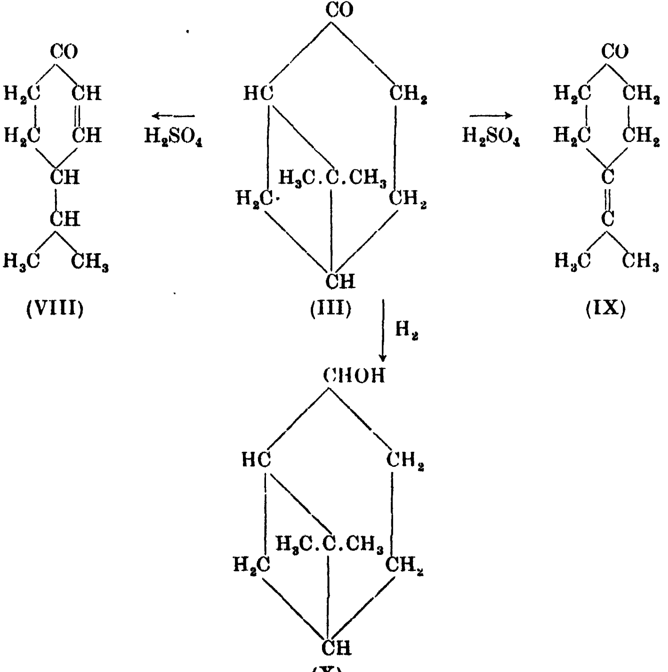
[¶] *Ibid.* 1924, **437**, 188.

[**] *Annalen*, 1907, **356**, 231.

by the action of dilute sulphuric acid into 4-iso*propyl*-Δ²-cyclo*hexenone* (VIII), which, if concentrated acid is used, is accompanied by the isomeric ketone, iso*propylidene*cyclo*hexan*-4-*one* (IX).*


(VI)


(VII)


(VIII) (III) (IX)

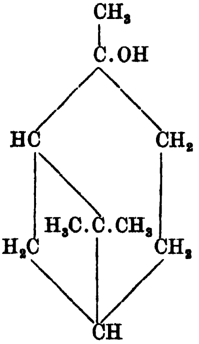
(X)

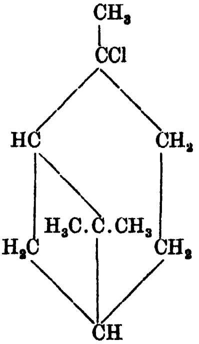
On reduction with sodium in moist ethereal solution nopinone yields a mixture of two alcohols, α- and β-nopinol (X).† These two alcohols are probably stereoisomerides. *α-Nopinol*, m.p. 102°, b.p. 204–205°, $[\alpha]_D$ −5·32° (in ether), yields a *phenylurethane*, m.p. 131–132°, whilst *β-nopinol* is an oil, $[\alpha]_D$ −15·03° (in ether), the *phenylurethane* melting at 95–96°. Nopinone has been used in a number of synthetical investigations, the most important of which was that which culminated in a partial synthesis of β-pinene. Wallach[*] showed that, when the ketone was treated with methyl magnesium iodide, *l-methylnopinol* (XI), m.p. 58–59°, b.p. 204–205°, $[\alpha]_D$ −4·99°, was obtained. It was not however found possible to dehydrate this. With phosphorus pentachloride a *monochloride*, b.p. 95–105°/12 mm., is formed, which was considered by Wallach to be *pinene hydrochloride* (XII), but in view of the instability of this substance (see p. 172) this is undoubtedly incorrect, and the substance was probably *dipentene monohydrochloride* (XIII), since it is known[†] that dipentene is formed by the action of hydrogen chloride on methylnopinol.

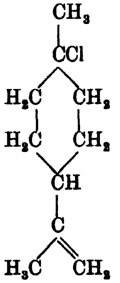
---

* Rimini, *Gazzetta*, 1916, **46**, II, 119.

† Wallach and Blumann, *Annalen*, 1907, **356**, 236.


(XI)


(XII)


(XIII)

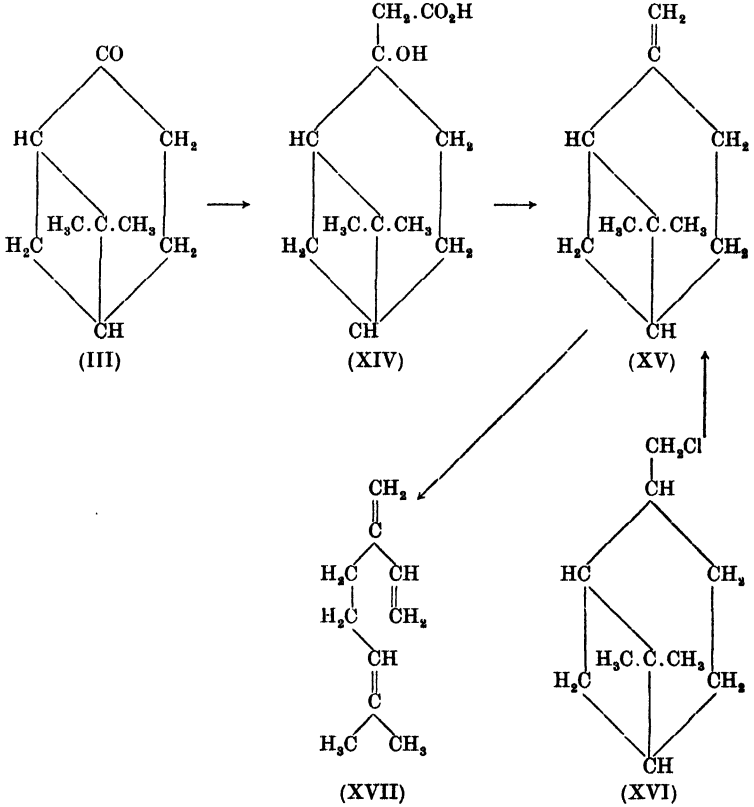
Wallach[‡] succeeded, however, in effecting a partial synthesis of β-pinene from nopinone by another process. By condensation of the ketone with ethyl bromoacetate in the presence of zinc, *ethyl nopinolacetate* was prepared, which on hydrolysis gave the corresponding *hydroxy acid* (XIV). Distillation of the crude acid under diminished pressure yields a terpene, b.p. 155–161°, $d^{20°}$ 0·863, $n_D^{20°}$ 1·4699, $[\alpha]_D$ +15·93°, consisting essentially of l-*α-fenchene* (p. 538). If, however, the pure acid, m.p. 83–85°, is dehydrated with sodium hydrogen sulphate, pure l-β-*pinene* (XV) is obtained. The synthetic hydrocarbon boiled at 162–163°, $d^{22°}$ 0·8660, $n_D^{22°}$ 1·4724, $[\alpha]_D$ $-22{\cdot}2°$, and its constitution was established by oxidation to *l*-nopinic acid, m.p. 126–127°, $[\alpha]_D$ $-16{\cdot}02°$.

---

[*] *Annalen*, 1907, **356**, 234; 1908, **360**, 88.

[†] Lipp and Steinbrink, *J. pr. Chem.* 1937 [ii], **149**, 107.

[‡] *Annalen*, 1907, **357**, 49; 1908, **363**, 9.



Although a partial synthesis of β-pinene had thus been achieved, there was no *direct* evidence of the presence of a *cyclo*-butane ring in nopinone, since neither nopinone nor β-pinene yield on oxidation any acids of the pinic acid series. The ready conversion of β-pinene into α-pinene afforded, however, very strong evidence of the correctness of the dicyclic structure. It is only recently that β-pinene has been synthesised* by the elimination of hydrogen chloride from 7-chloropinane (XVI) (see p. 104). Although several attempts have been made, nopinone has not yet been prepared synthetically.[*]

---

* Bonnet, *Bull. Inst. Pin*, 1938, pp. 217, 241; 1939, p. 1.

Dupont[†] has prepared very pure *l*-β-pinene by the fractional distillation of French oil of turpentine. The constants of the hydrocarbon from this source, $d^{15°}$ 0·874, $n_D^{15°}$ 1·4872, $[\alpha]_D - 22·44°$, are in good agreement with those found by Wallach for the synthetic terpene. It crystallises at $-75°$ with a velocity of 196 mm. per minute.

The rotatory dispersion has been studied by Servant[‡] and by Padmanabhan and Jatkar.[§]

β-Pinene is usually identified by oxidation to nopinic acid, the characteristic sparingly soluble sodium salt of which can be readily separated; the most suitable conditions for carrying out this oxidation have been described by Dupont and Brus.[‖]

In its general reactions β-pinene resembles very closely α-pinene, but investigation is hampered by the difficulty of effecting a complete separation of the two hydrocarbons. The only convenient method is prolonged fractional distillation, although Austerweil[¶] has suggested taking advantage of the greater solubility of β-pinene in alcohol. In 72 per cent. alcohol α-pinene has a solubility of 2 per cent. and β-pinene of 9 per cent., whilst in 65 per cent. alcohol at 15° it is 0·6 and 3·3 per cent., respectively. If large quantities of material are available, this process could probably be applied successfully. A further difficulty in investigating the reactions of β-pinene lies in the great tendency which it shows to isomerise to α-pinene. Austerweil[**] has shown that, when it is heated with rosin at 160° for 15 to 20 hours, over 70 per cent. is isomerised. The change does not appear to be reversible and other catalysts are even more effective, since Richter and Wolff[††] have found that when β-pinene is shaken with platinum black, which has been previously saturated with hydrogen, a similar isomerisation occurs. When heated under pressure at 270° polymerisation to a *diterpene*, b.p. 170–185°/10 mm., $d^{20°}$ 0·8950, $n_D^{20°}$ 1·5095, $[\alpha]_D$ $-3·5°$, occurs.[*]

---

[*] Compare Perkin and Simonsen, *J.C.S.* 1907, **91**, 1736; Guha and Ganapathi, *Ber.* 1936, **69**, 1185.

[†] *Ann. Chim.* 1924 [x], **1**, 184; compare Darmois, *ibid.* 1911 [viii], **22**, 527; Pariselle, *Compt. rend.* 1921, **172**, 1496; Fuguitt, Stallcup and Hawkins, *J. Amer. C.S.* 1942, **64**, 2978.

[‡] *Compt. rend.* 1932, **194**, 368.

[§] *J. Ind. C.S.* 1935, **12**, 518.

[‖] *Ann. Chim.* 1923 [ix], **19**, 186; cf. Dupont, *Bull. Inst. Pin*, 1929, p. 269.

[¶] *G.P.* 427418.

[**] *Bull. Soc. chim.* 1926 [iv], **39**, 1643.

[††] *Ber.* 1926, **59**, 1733.

The thermal isomerisation of β-pinene in the vapour phase over glass at 350° gives a 70 per cent. yield of myrcene (XVII) together with a small amount of limonene. Unlike α-pinene (see p. 134) it gives no *allo*-ocimene.[†]

Vavon[‡] and Lipp[§] have shown that on catalytic hydrogenation β-pinene behaves like α-pinene and yields pinane (p.)102—a further proof that the two hydrocarbons contain the same ring structures.

On autoxidation in the presence of catalysts β-pinene yields a mixture of d-*pinocarveol*, l-*myrtenol* and l-*myrtenal*.[‖] Oxidation with selenium dioxide gives d-*pinocarveol*, d-*pinocarvone* and l-*myrtenal*.[¶] The names of the products have been corrected in accordance with the findings of Schmidt[**] (see p. 221); it is not unlikely that *l*-myrtenol also is present. The first pair are evidently formed by normal α-methylenic oxidation, whilst the myrtenol can be accounted for most readily by assuming a partial isomerisation of β-pinene into α-pinene during the reaction.

The oxidation of β-pinene with ozone has been investigated by Brus and Peyresblauques[††] and by Schmidt.[‡‡] The ozonolysis proceeds smoothly and in the manner anticipated, yielding formaldehyde and nopinone in a yield of approximately 50 per cent. A small quantity of a *lactone*, $C_9H_{14}O_2$, m.p. 126–127°, is also formed; the constitution of this has not been determined. The *d*-nopinone, so obtained, is probably optically pure, since in these independent investigations the rotatory powers of the ketone were $[\alpha]_D$ $+18·2°$ and $+18·4°$ respectively.

Henderson and Chisholm[§§] have examined the products which are formed when β-pinene is oxidised with hydrogen peroxide. The oxidation proceeds in a somewhat different manner to that of α-pinene (p. 142), yielding a mixture of *borneol* (XIX), *fenchyl*

---

[*] Semmler and Jonas, *Ber.* 1913, **46**, 1567; 1914, **47**, 2078.

[†] Goldblatt and Palkin, *J. Amer. C.S.* 1941, **63**, 3517; U.S.P. 2420131; compare Arbusov, *Brit. Chem. Abstr.* A, 1936, p. 607.

[‡] *Compt. rend.* 1910, **150**, 1127, 1428.

[§] *Ber.* 1923, **56**, 2098.

[‖] Schmidt, *Ber.* 1930, **63**, 1130; *Chem. Zentr.* 1942, I, 2531.

[¶] Stallcup and Hawkins, *J. Amer. C.S.* 1941, **63**, 3339; 1942, **64**, 1807; Joshel and Palkin, *ibid.* 1942, **64**, 1008; compare Dupont, Allard and Dulon, *Bull. Soc. chim.* 1933 [iv], **53**, 599; Zacharewicz, *Chem. Zentr.* 1938, I, 3206.

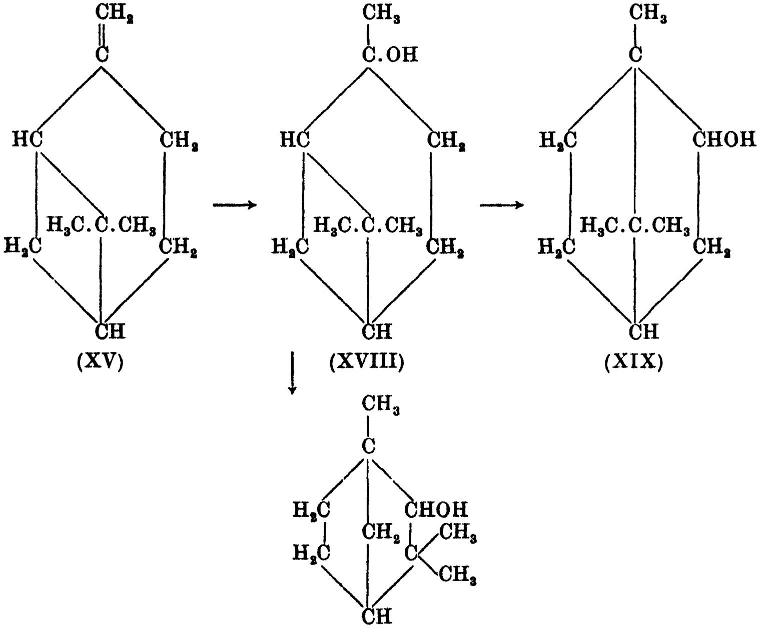
[**] *Loc. cit.*

[††] *Compt. rend.* 1928, **187**, 984; Brus, *Bull. Inst. Pin*, 1929, p. 271.

[‡‡] *Z. angew. Chem.* 1929, **42**, 126.

[§§] *J.C.S.* 1924, **125**, 107.

alcohol (XX), and possibly a polyhydric alcohol, which was not investigated. Hydrogen peroxide acts, therefore, as a hydrating agent, since both borneol and fenchyl alcohol result from the hydration of oil of turpentine.* The mechanism of the formation of these alcohols from the primary hydration product (XVIII) has already been discussed (p. 156).



(XV) (XVIII) (XIX) (XX)

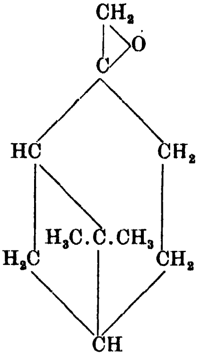
By the oxidation of β-pinene with perbenzoic acid, *β-pinene oxide* (XXI), b.p. 98–99°/33 mm., $d_{4°}^{21°}$ 0·963, $n_D^{21°}$ 1·4756, $[\alpha]_D^{16°}$ +2·9°, may be obtained.† By distillation over pumice, or by heating with zinc chloride, it is converted into *dihydromyrtenal* (XXII), b.p. 207–208°, $d^{15°}$ 0·9623, $n_D^{15°}$ 1·4812 (*semicarbazone*, m.p. 152–153°). The oxide reacts with methyl magnesium iodide to give a product, b.p. 132–134°/30 mm., $d_{20°}^{20°}$ 0·9676, $n_D^{20°}$ 1·4887, which was considered by Prileschaev and Prokoptschuk to be

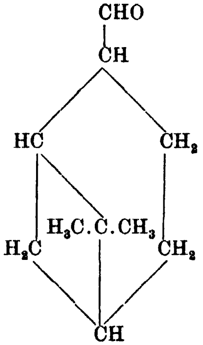
---

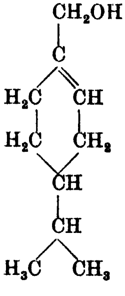
* Compare Bouchardat and Lafont, *Compt. rend.* 1898, **126**, 756; Barbier and Grignard, *Bull. Soc. chim.* 1909 [iv], **5**, 512, 519.

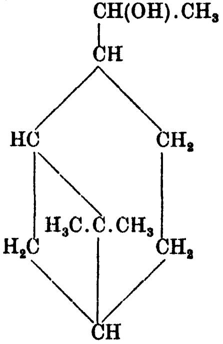
† Faidutti, *Compt. rend.* 1929, **189**, 855; Prileschaev and Prokoptschuk, *Chem. Zentr.* 1934, II, 2386; Arbusov, *ibid.* 1939, II, 1079.

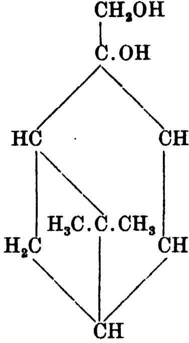
Δ^1-*p*-menthen-7-ol (XXIII), but this is most unlikely, and it is more probably *dihydromyrtenylmethylcarbinol* (XXIV), formed from the intermediate dihydromyrtenal.


(XXI)


(XXII)


(XXIII)


(XXIV)


(XXV)

Although the main product formed by the oxidation of β-pinene with potassium permanganate is *l*-nopinic acid, which according to Brus[*] is optically pure, $[\alpha]_D$ $-15{\cdot}8°$ (in alcohol $c = 10$), two other products, nopinone and β-pinene glycol (XXV), m.p. 76–78°, are also formed. The glycol was first prepared by Wagner[†] by oxidation of oil of turpentine, and its derivation from β-pinene was subsequently established by Wallach.[‡] When it is warmed with dilute acids it gives a mixture of *pinol* and an *aldehyde* which is probably dihydromyrtenal (XXII) though this has not been confirmed.

[*] *Compt. rend.* 1924, **179**, 501.

[†] *Ber.* 1894, **27**, 2274.

[‡] *Annalen*, 1908, **363**, 11.

Henderson and Chisholm[*] have shown that with chromyl chloride β-pinene reacts in a similar manner to α-pinene, yielding an additive compound, $C_{10}H_{16}$, $2CrO_2Cl_2$, which is decomposed by water, yielding a *ketone*, $C_9H_{14}O$, identical with that prepared from α-pinene (p. 144); in addition, a mixture of aldehydes and dl-trans-*pinolglycol*, m.p. 125°, is formed.

β-Pinene does not yield any crystalline dihalogen derivatives, the action of chlorine and bromine giving, as Brus[†] has shown, bornyl chloride and bromide respectively. These are evidently secondary products formed by the action of the hydrogen halides on the hydrocarbon, since it has been shown by many investigators[‡] that with the halogen acids β-pinene behaves in exactly the same manner as α-pinene (p. 170). Aschan[§] has shown that β-pinene yields, when treated with hydrogen chloride at a low temperature (compare p. 171), pinene hydrochloride. Since this substance yields on treatment with aniline α-pinene, this is a direct synthesis of α-pinene from β-pinene.

With hypochlorous acid β-pinene reacts in a similar manner to α-pinene. Henderson and Kerr[‖] have prepared by the action of this reagent three crystalline dichlorohydrins, which are probably *dichloro*-p-*menthanediols*; they melt at 135°, 166° and 131° respectively. Owing to the poor yield and the difficulty of separating these isomerides it has not proved possible to determine their constitution, but the dichlorohydrin, m.p. 135°, is possibly represented by (XXVI) since both the hydroxy groups appear to be tertiary, and on treatment with alkali it yields a *monochlorohydrin*, m.p. 125°, probably (XXVII), since it is not identical with pinol monochlorohydrin.

Considerable attention has been devoted to the subject of the hydration of β-pinene, and there has been much discussion, especially amongst the French workers, as to whether α- and β-pinene behave similarly on treatment with hydrating agents, dilute mineral acids and organic acids. As has been mentioned already (p. 165), α-pinene yields a mixture of monocyclic terpenes, α-terpineol, borneol and fenchyl alcohol, and it has been

---

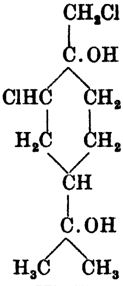
[*] *J.C.S.* 1924, **125**, 107.

[†] *Compt. rend.* 1928, **186**, 240.

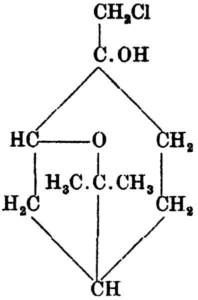
[‡] *Inter al.*, Wallach, *Annalen*, 1908, **363**, 9; Pariselle, *Compt. rend.* 1921, **172**, 1496.

[§] *Naphtenverbindungen, Terpene und Campherarten*, p. 195.

[‖] *J.C.S.* 1924, **125**, 103.



(XXVI)



(XXVII)

suggested that the dicyclic alcohols are formed in greater amount from β-pinene. The most recent experiments, which have been carried out by Austerweil and his collaborators using[*] benzoic acid as the hydrating agent, have led to the conclusions (i) that in all cases of hydration β-pinene is partially converted into α-pinene, (ii) that the hydration of α- and β-pinenes gives products which are qualitatively the same, but quantitatively different. With β-pinene the dicyclic alcohols, borneol, *iso*borneol and fenchyl alcohol are the main products, comparatively little α-terpineol (and monocyclic hydrocarbons) being formed. This factor is one of considerable technical importance in view of the use of *iso*borneol for the preparation of synthetic camphor.

Whilst dilute mineral acids hydrate β-pinene, Brooks and Humphrey[†] have shown that, with concentrated sulphuric acid (85 per cent.) at 0°, polymerisation occurs with the formation of hydrocarbons of the composition $C_{20}H_{32}$ and $C_{30}H_{48}$. In connection with the hydration of β-pinene it is of interest to note that Delépine and Adida[‡] have found that with picric acid β-pinene reacts in exactly the same way as α-pinene, yielding bornyl and fenchyl picrates.

Although the fact was not recognised until much later, the first true derivative of β-pinene was prepared by Pesci and Bettelli,[§] who obtained *β-pinene nitrosite* (XXVIII) by the action of nitrous acid on oil of turpentine. When this substance, which was an oil, was distilled in steam, a strongly laevorotatory liquid

---

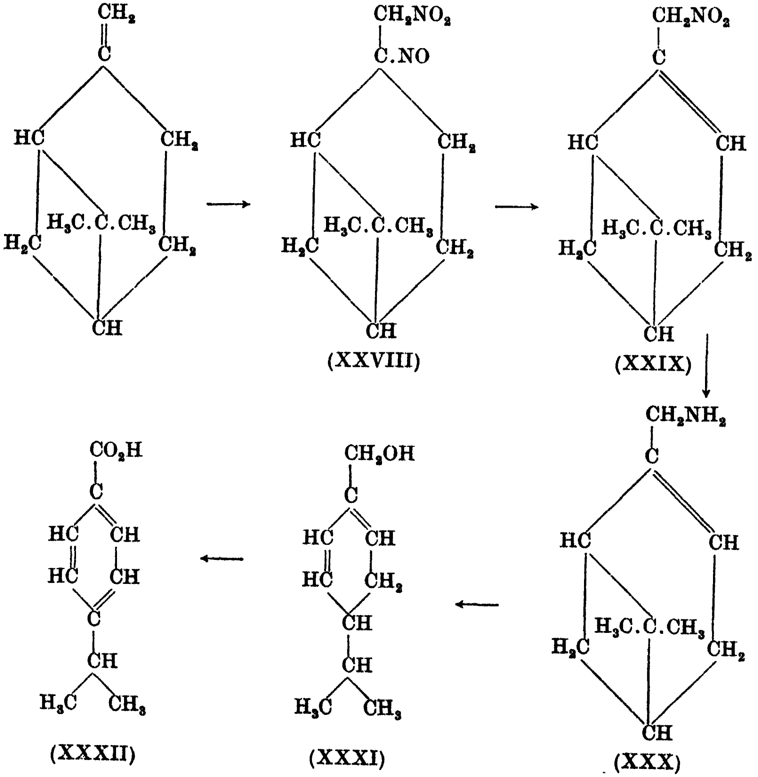
[*] *Bull. Soc. chim.* 1926 [iv], **39**, 690, 1732; 1927 [iv], **41**, 1088, 1507; 1930 [iv], **47**, 1157; compare *inter al.*, Wallach, *Annalen*, 1908, **363**, 9; Dupont, *Chim. et Ind.* 1922, **8**, 555; Delépine, *Compt. rend.* 1924, **178**, 2087.

[†] *J. Amer. C.S.* 1918, **40**, 844.

[‡] *Bull. Soc. chim.* 1926 [iv], **39**, 782.

[§] *Gazzetta*, 1886, **16**, 337.

"nitroterebenthine", was obtained. This reaction was studied subsequently by Wallach and Isaac,* who found that *nitropinene* (nitroterebenthine) (XXIX) gave on reduction with zinc dust in acetic acid solution an amine, *aminopinene* (XXX), b.p. 95°/12 mm., d^{19° 0·9325, $n_D^{19^\circ}$ 1·4960, which was laevorotatory and could be characterised by the preparation of the crystalline *trimethylammonium iodide*, m.p. 198°. Aminopinene is very unstable and yields, with nitrous acid, the monocyclic *alcohol* (XXXI) which gives on oxidation with chromic acid a mixture of cuminaldehyde and *cumic acid* (XXXII). Although the constitutions of nitropinene and its derivatives have not been rigidly proved, there would appear to be little doubt that the reactions outlined above proceed in accordance with the following scheme:



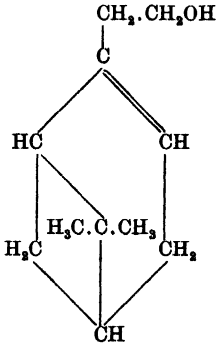
(XXVIII) (XXIX) (XXX) (XXXI) (XXXII)

---

* *Annalen*, 1906, **346**, 243.

An addition compound of β-pinene with hydroferrocyanic acid has been described by Stephen and Hammerich.*

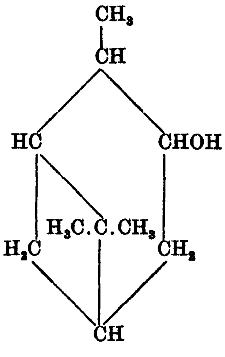
β-Pinene condenses with formaldehyde to give the alcohol (XXXIII), b.p. 110·5°/10 mm., $d_{4°}^{25°}$ 0·9647, $n_D^{25°}$ 1·4920, $\alpha_D^{25°}$ − 36·5°, which has been termed "*nopol*";† the formation of this substance involves a migration of the ethylenic linkage into the ring.



(XXXIII)

B. ALCOHOLS

PINOCAMPHEOL



The secondary alcohol, *l*-pinocampheol, has been found by Rutovski and Vinagradova‡ to occur in oil of hyssop (from

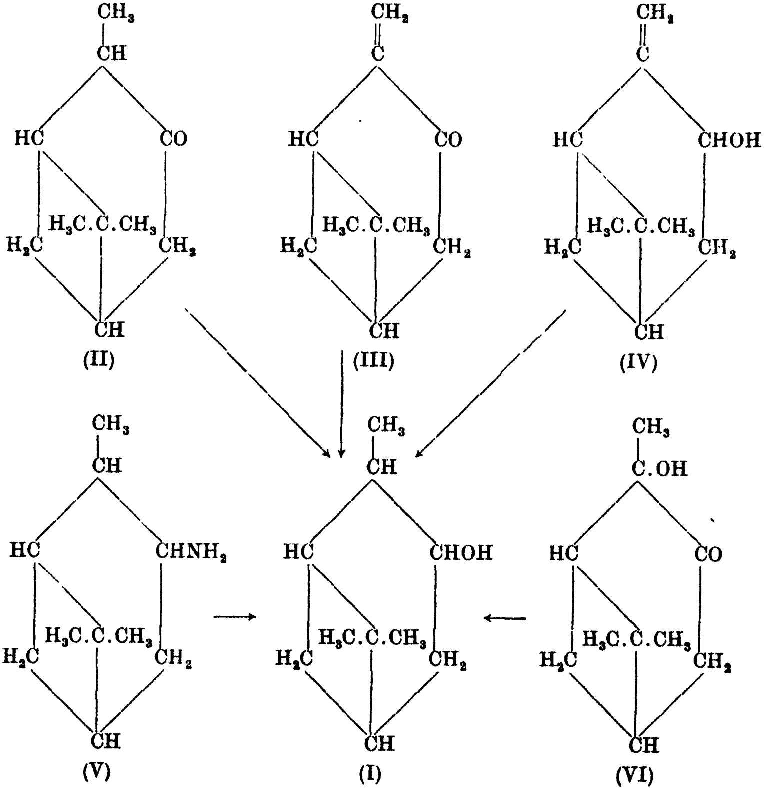
---

* *J. pr. Chem.* 1931 [ii], **129**, 285.

† Bain, *J. Amer. C.S.* 1946, **68**, 638.

‡ *Trans. sci. chem-pharm. Inst. Moscow*, 1924 [10], 22.

Hyssopus officinalis). *dl*-Pinocampheol (I) was prepared by Wallach and Smythe[*] by the reduction of *dl*-pinocamphone (II) (p. 231) with sodium in moist ethereal solution, by the reduction of pinocarvone (III)[†] and by the catalytic hydrogenation of dl-*pinocarveol* (IV) (p. 222).[‡] Tilden and Shepheard[§] have also described its preparation from *pinocamphylamine* (V) by the action of nitrous acid. Later, *l*-pinocampheol was prepared by Gildemeister and Köhler[||] by the reduction of *l*-pinocamphone, and it has also been obtained by the reduction of *l*-1-hydroxy-pinocamphone (VI) with sodium and alcohol.[¶]



---

[*] *Annalen*, 1898, **300**, 288.

[†] Wallach, *Annalen*, 1906, **346**, 231; the ketone was at that time termed carvopinone (see p. 240).

[‡] Wallach and Ost, *Annalen*, 1912, **389**, 185.

[§] *J.C.S.* 1906, **89**, 1563.

[||] *Wallach Festschrift*, 1909, p. 414.

[¶] Kuwata, *J. Amer. C.S.* 1937, **59**, 2509.

The constitution of pinocampheol follows directly from its preparation by the reduction of pinocamphone and its conversion into this ketone on oxidation.

dl-Pinocampheol, as usually prepared, has b.p. 218–219°, $d^{20°}$ 0·965, $n_D^{20°}$ 1·4861, and is an oil with an odour resembling that of α-terpineol, whilst the laevorotatory alcohol, prepared by Gildemeister and Köhler, is crystalline, m.p. 67–68°, b.p. 217–218°, $d^{15°}$ 0·9678, $n_D^{15°}$ 1·4842, $[\alpha]_D$ −44·38°. The natural alcohol has somewhat different constants, m.p. 56–57°, $d^{20°}$ 0·9501, $n_D^{20°}$ 1·4888, $[\alpha]_D$ −45·63°, and is a stereoisomeride of that prepared from *l*-pinocamphone.

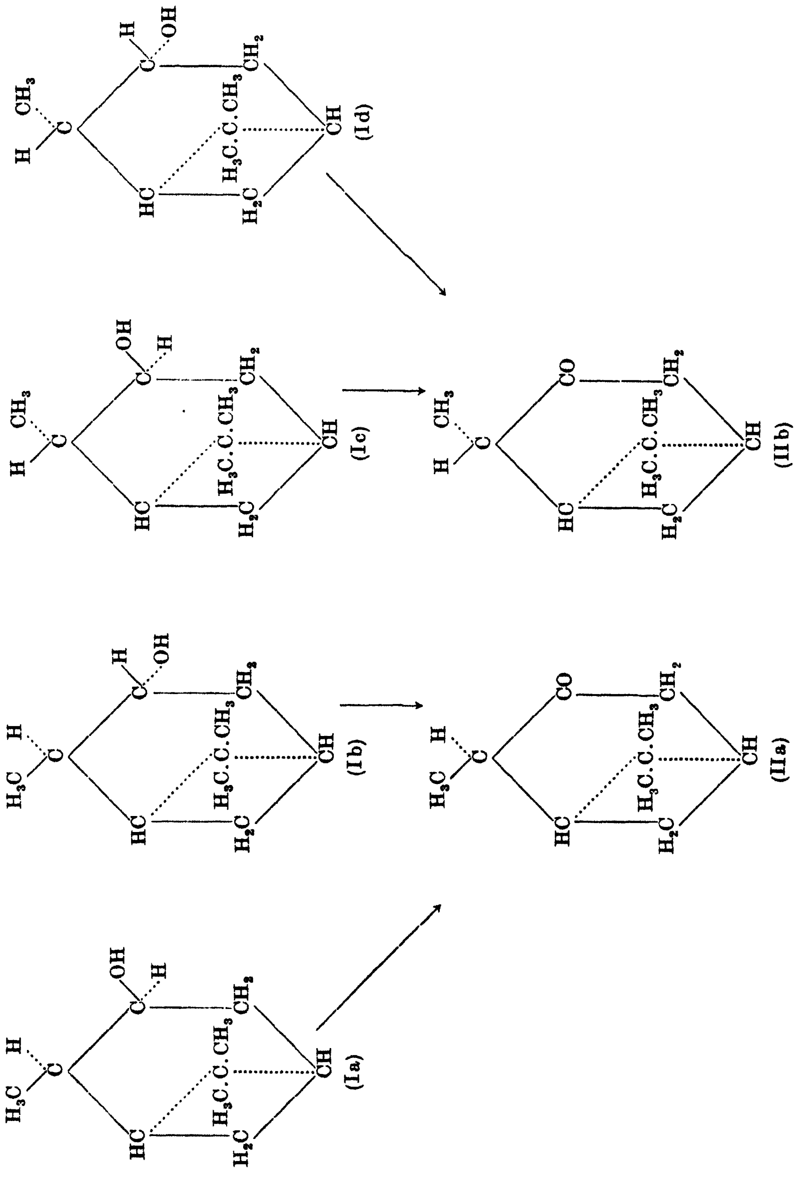
The configurational relationships of the optically active and inactive alcohols have only recently been investigated. Pinocampheol can exist in the four stereoisomeric forms (Ia–d), all of which have now been isolated by Schmidt;* following the nomenclature adopted in the menthol series (Vol. I, p. 233) these have been named *pinocampheol*, neo*pinocampheol*, iso*pinocampheol*, and neoiso*pinocampheol*, respectively. On oxidation, the first pair both give pinocamphone (IIa), whilst (Ic) and (Id) give *iso*pinocamphone (IIb) (see p. 208), and this evidence, taken in conjunction with studies on the rates of saponification of esters, and of dehydration of the alcohols, leads to the particular allocations of structures shown in the formulae on p. 208.

Pinocampheol (Ia) is formed predominantly by reduction of either pinocamphone or *iso*pinocamphone with sodium and alcohol; if, on the other hand, pinocamphone is hydrogenated over nickel at 130°, *neo*pinocampheol can be isolated from the reaction products by virtue of the sparing solubility of its hydrogen phthalate. *iso*Pinocampheol and *neoiso*pinocampheol are obtained in practically pure condition by hydrogenation of *trans*- and *cis*-pinocarveols (p. 222) respectively; *l*-*iso*pinocampheol is identical with the natural alcohol. The properties of the stereoisomerides, and of some derivatives, are given in the table on page 209.†

---

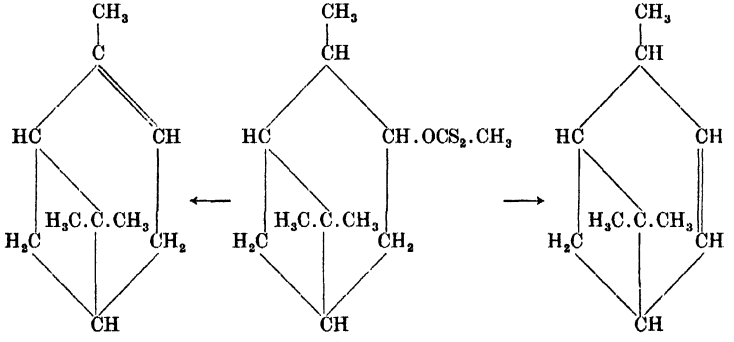
* Schmidt and Schulz, *Schimmel's Report*, 1934, p. 97; Schmidt, Schulz and Doll, *ibid.* 1940, p. 38; Schmidt, *Ber.* 1944, 77, 544.

† Bonnet (*Bull. Inst. Pin*, 1938, p. 241) has obtained a pinocampheol, m.p. 58–59°, *hydrogen phthalate*, m.p. 109–110°, from 2-chloropinane, but its stereochemical homogeneity is doubtful.


(Id)
(Ic)
(IIb)
(Ib)
(IIa)
(Ia)

						M.p. of derivative			
Pinocampheol	M.p.	B.p.	$d^{20°}_{15°}$	$n^{20°}$	$[\alpha]_D$ in benzene	Phenyl-urethane	α-Naphthyl-urethane	Hydrogen phthalate	*p*-Toluene-sulphonate
d- and *l*-	67°	217°	0·9725	1·4877	±72°	77°	91°	111°	72°
dl-	36°	217°	0·9680	—	± 0°	99°	—	113°	—
d- and *l*-*neo*-	27°	215°	0·9735	1·4882	±17°	Liq.	148°	147°	73°
dl-*neo*-	11°	—	—	—	± 0°	—	—	—	—
d- and *l*-*iso*-	57°	219°	0·9720	1·4865	±32°	Liq.	88°	126°	Liq.
dl-*iso*-	42°	219°	0·9730	1·4856	± 0°	—	—	—	—
d-*neoiso*-	48°	217°	0·9770	1·4920	+36°	Liq.	88°	126°	73°

A dl-*methylxanthate* (VII), m.p. 60·5–61°, was prepared by Tschugaev,* the corresponding laevorotatory derivative, m.p. 36–37°, having been described by Gildemeister and Köhler. The methylxanthate decomposes when heated to 170–190°, yielding a mixture of *α-pinene* (VIII) and *δ-pinene* (IX), the hydrocarbons prepared from the optically active xanthate being slightly active.



(VIII) (VII) (IX)

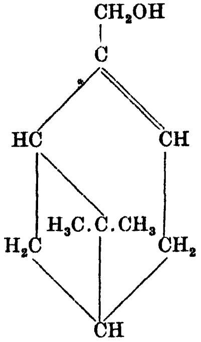
The presence of these two terpenes was proved (i) by the preparation of pinene nitrosochloride, and (ii) by oxidation with potassium permanganate, when a mixture of pinonic acid and pinocamphoric acid was obtained. Although, according to Gildemeister and Köhler, very little α-pinene is formed, the reaction is of particular interest, since it afforded the first partial synthesis of this important hydrocarbon. A similar mixture is obtained by the action of sodium ethoxide on pinocamphyl *p*-toluene sulphonate.†

---

* *J. Russ. Phys. Chem. Soc.* **1907, 39,** 1330.

† Schmidt, *Chem. Ber.* **1947, 80,** 520.

MYRTENOL



The primary unsaturated alcohol, *d*-myrtenol, $C_{10}H_{16}O$, was separated from the essential oil derived from the leaves and flowers of *Myrtus communis* L. (myrtle oil) by Soden and Elze[*] and its constitution was determined by Semmler and Bartelt,[†] who showed it to be a derivative of α-pinene.

More recently it has been isolated from the essential oil present in *Darwinia grandiflora* and other shrubs[‡] from *Chamaecyparis formosensis* Matsum (accompanied in this instance by *dihydromyrtenol*[§]) and from *Eucalyptus globulus.*[‖]

The alcohol was isolated from the higher boiling fraction of the oils by taking advantage of the facility with which it combines with phthalic anhydride to yield a crystalline *hydrogen phthalate*,[¶] from which it can be regenerated by hydrolysis with alkali. The constitution was determined by two distinct methods.

When the alcohol, dissolved in light petroleum, was treated with phosphorus pentachloride a chloride, d-*myrtenyl chloride*, b.p. 90°/12 mm., $d^{20°}$ 1·015, n_D 1·4976, $[\alpha]_D$ $+24°$, was obtained, which on reduction with sodium and alcohol gave mainly *d*-α-pinene, together with a small quantity of *myrtenyl ethyl ether*, b.p. 80–85°/10 mm., $d^{20°}$ 0·899, n_D 1·4725. This result was most simply explained if *d*-myrtenol was assumed to be the primary alcohol (II), when *d*-myrtenyl chloride would be (III) giving on reduction *d*-α-pinene (IV).

---

[*] *Chem.-Ztg.* 1905, **29**, 1031.

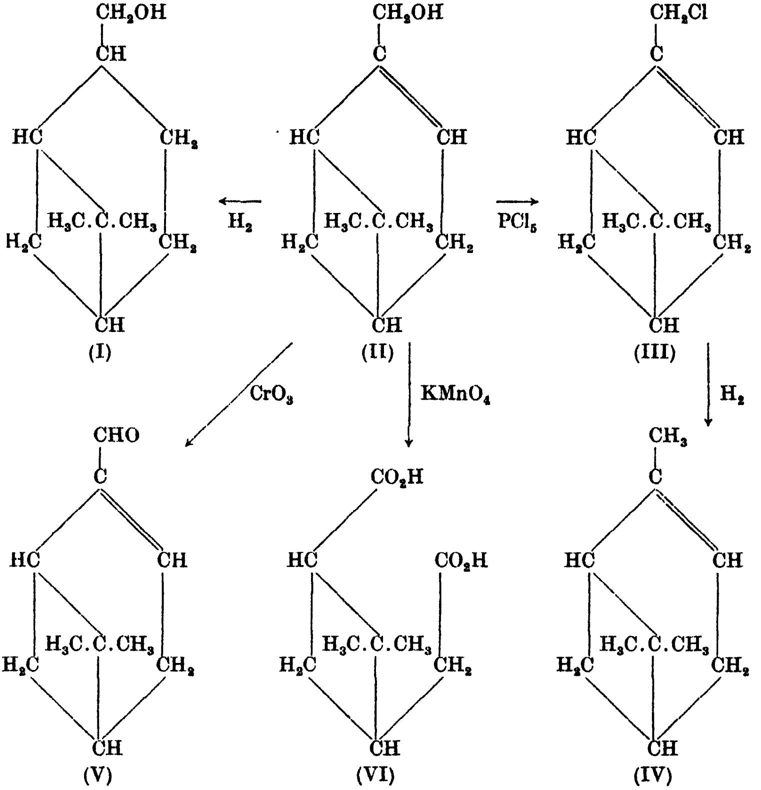
[†] *Ber.* 1907, **40**, 1363.

[‡] Penfold, Ramage and Simonson, *J. Proc. Roy. Soc. New South Wales*, 1934, **68**, 36.

[§] Kafuku and Ichikawa, *Bull. C.S. Japan*, 1933, **8**, 371; Sebe, *ibid.* 1938, **59**, 1285; 1941, **62**, 22.

[‖] Schmidt, *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530.

[¶] Compare Rupe and Héritier, *Annalen*, 1927, **459**, 171.



Confirmation of the presence of the primary alcohol group in *d*-myrtenol was obtained by its oxidation with chromic acid to the aldehyde, d-*myrtenal* (V), which was subsequently isolated by Semmler and Zaar* from false camphor wood oil (see p. 223), whilst the presence of the *cyclo*butane ring was established by its oxidation with potassium permanganate to d-*pinic acid* (VI).

d-, *l*- and *dl*-Myrtenols have been obtained by cautious oxidation of the appropriate α-pinene with selenium dioxide (p. 139) and by the autoxidation of β-pinene (p. 199). The alcohol may also be present in the products of the autoxidation of α-pinene,* and in those obtained by the oxidation of β-pinene with selenium dioxide (p. 199).

---

* *Ber.* 1911, **44**, 815.

d-Myrtenol can be readily separated and identified by the preparation of the *phenylurethane*, m.p. 58–59°, the *α-naphthylurethane*, m.p. 92–93°† or the *hydrogen phthalate*, m.p. 114–115°, $[\alpha]_D$ $+21{\cdot}36°$ (in ethyl alcohol). The *dl*-hydrogen phthalate has m.p. 120°. It can be identified also by oxidation to *d*-myrtenal, from which a number of crystalline derivatives can be prepared (see p. 226).

d-Myrtenol is an oil having a pleasant odour reminiscent of myrtle oil. After purification through the hydrogen phthalate, it boils at 222–224°, 105·5°/9 mm., $d^{20°}$ 0·9763, n_D 1·4966, $[\alpha]_D$ $+49{\cdot}7°$. When heated at 280° under pressure it resinifies.

For *l*-myrtenol, the following constants have been observed:‡ b.p. 221–222°, $d^{15°}$ 0·985, n_D 1·4968, $[\alpha]_D$ $-46°$ (*naphthylurethane*, m.p. 92–93°).

d-Myrtenol is not reduced by sodium and amyl alcohol, but with sodium and xylene it gives l-trans-*dihydromyrtenol* (I), b.p. 127°/22 mm., $[\alpha]_D$ $-26°$ (*hydrogen phthalate*, m.p. 109°, $[\alpha]_D$ $-15°$; the *dl-trans*-hydrogen phthalate has m.p. 114–116°). Hydrogenation of *d*-myrtenol over platinum gives d-cis-*dihydromyrtenol*, b.p. 122°/20 mm., $[\alpha]_D$ $+18°$; l-cis-*dihydromyrtenol* shows $[\alpha]_D$ $-24{\cdot}5°$ and gives a *hydrogen phthalate*, m.p. 124°, $[\alpha]_D$ $-5{\cdot}6°$; the *dl-cis*-hydrogen phthalate has m.p. 127°. The configurations were deduced from the Raman spectra of the products.§ A direct comparison between these substances and the natural dihydromyrtenol would be of interest. The product obtained from 7-chloropinane (VII) by Bonnet‖ had b.p. 81–82°/3 mm., $d_{4°}^{20°}$ 0·9860, $n^{20°}$ 1·4924, $[\alpha]_D$ $+12{\cdot}5°$ (*hydrogen phthalate*, m.p. 120°) and was probably *d-cis*-dihydromyrtenol; on oxidation it gave *dihydromyrtenal* (p. 224).

According to Zacharewicz,¶ myrtenol on cautious oxidation with potassium permanganate gives the *glycerol* (VIII), *d*- and *l*-, m.p. 67–68°, $[\alpha]_D$ $\pm 10{\cdot}6°$; *dl*-, m.p. 71·5°.

---

* Dupont and Zacharewicz, *Compt. rend.* 1934, **198**, 1699; 1935, **200**, 759.

† Penfold, Ramage and Simonsen, *loc. cit.*

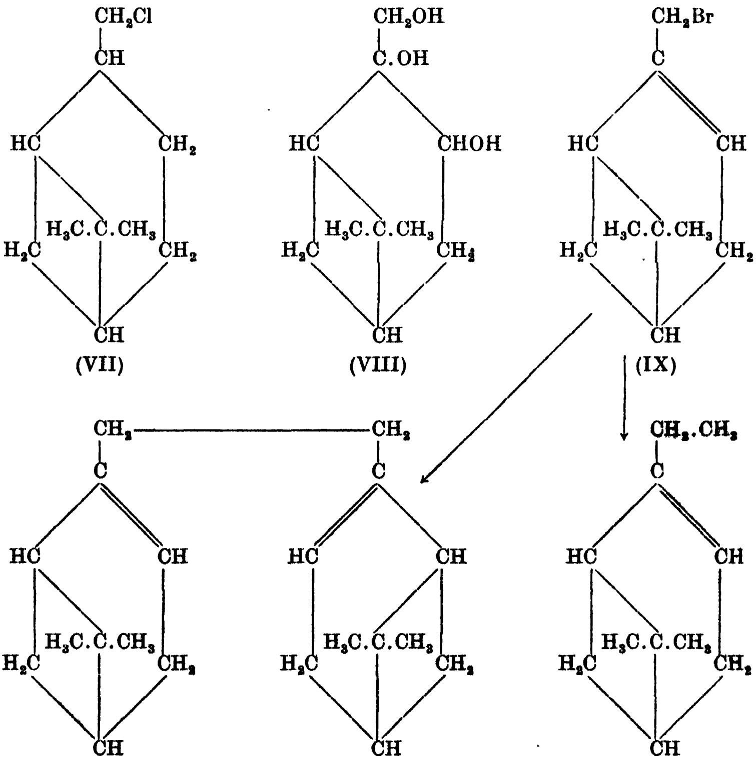
‡ Schmidt, *Schimmel's Report*, 1941, p. 70; *Chem. Zentr.* 1942, I, 2531.

§ Dupont and Zacharewicz, *Compt. rend.* 1934, **199**, 365.

‖ *Bull. Inst. Pin*, 1938, p. 241.

¶ *Chem. Zentr.* 1938, I, 3206.

With the halogens, myrtenol gives no crystalline derivatives, whilst with hydrogen chloride it was found by Semmler and Bartelt to form an oil, b.p. 127–135°/10 mm., which they considered to be an additive compound, but the composition of this derivative has not been determined. As mentioned above, the alcohol reacts readily with the phosphorus halides, and by the action of phosphorus tribromide in ethereal solution Rupe and Héritier have prepared d-*myrtenyl bromide* (IX), b.p. 93°/9 mm., $[\alpha]_D$ +32·31°. The *l*-bromide, $[\alpha]_D$ −35°, has been described by Buu-Hoï, Hiong-Ki-Wei, Lecomte and Royer.* This bromide does not give a magnesium derivative, but when treated with the metal in ethereal solution a Wurtz-Fittig reaction occurs with the formation of d-*dimyrtenyl* (X), b.p. 173–174°/10 mm., $d^{20°}$ 0·9521,


(VII) (VIII) (IX)

(X) (XI)

---

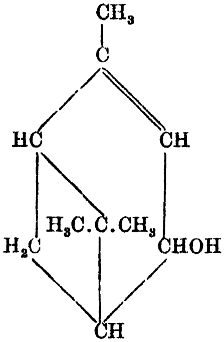
* *Bull. Soc. chim.* 1946 [v], **14**, 148.

$[\alpha]_D^{20^\circ}$ +13·79°. This reaction has been used by Rupe and Héritier for the preparation of homologues of α-pinene by treatment of myrtenyl bromide with alkyl magnesium halides, when substances of the type of d-*methylmyrtenyl* (homopinene) (XI), b.p. 95·5–96°/62 mm., d^{20° 0·8697, $[\alpha]_D^{20^\circ}$ +33·96°, were obtained. Myrtenyl bromide condenses readily with ethyl sodioacetoacetate to yield the corresponding substituted ethyl acetoacetate.

When *d*-myrtenol is boiled with dilute sulphuric acid (10 per cent.) a hydrocarbon, probably *p*-cymene, is obtained.

A large number of esters of *d*-myrtenol with various aliphatic and aromatic acids have been described by Rupe and his collaborators,[*] who found them to exhibit great regularity in their physical constants.[†]

VERBENOL



During an investigation of the essential oil derived from the gum-resin of *Boswellia Carterii*, Fromm and Autin[‡] separated an alcohol, olibanol, $C_{10}H_{16}O$, b.p. 200–220°, which was apparently a derivative of α-pinene, since it gave on oxidation pinononic acid (III) (p. 216). A subsequent investigation by Fromm and Klein[§] seemed to indicate that the fraction of olibanum oil boiling at about 200° was a mixture of alcohols (or ketones) which tended to isomerise when distilled at the ordinary pressure. They described three substances, α-, β- and γ-olibanols, only one of which,

---

[*] *Annalen*, 1915, **409**, 344.

[†] Compare Akermann, *ibid.* 1920, **420**, 23.

[‡] *Ibid.* 1913, **401**, 253.

[§] *Ibid.* 1921, **425**, 208.

β-olibanol, could be oxidised to pinononic acid. The exact conditions for separating these three substances and their relationship to one another were not clearly established. More recently, Blumann and Schulz* have shown the so-called olibanols to be a mixture of *d*-verbenone (p. 232), which was readily separated and characterised, and *d*-verbenol. The latter was not obtained pure, but it was identified by dehydration to *d*-verbenene (see below).

During their investigation of the autoxidation products of α-pinene (p. 139) Blumann and Zeitschel† observed that the higher boiling fraction of the oil, after removal of the verbenone, contained an alcohol or a mixture of alcohols. Owing to the marked tendency for elimination of water to occur, difficulty was experienced in the preparation of the pure alcohol, but ultimately partial success was achieved by the preparation of a liquid benzoate by the pyridine method. From the benzoate on hydrolysis an alcohol was obtained, that from the autoxidation of *d*-α-pinene having b.p. 102–103°/10 mm., $d^{20°}$ 0·9702, $n_D^{20°}$ 1·4890, $[\alpha]_D$ $+132{\cdot}30°$, and that from *l*-α-pinene, b.p. 102–103°/12 mm., $d^{20°}$ 0·9785, $[\alpha]_D$ $-50{\cdot}72°$. The former alcohol crystallised partially on cooling and was evidently not homogeneous. On oxidation of the alcohols in acetic acid solution with chromic acid, *d*- and *l*-verbenone (II) respectively were obtained, and there was therefore no doubt that they had the structure represented by (I), which was confirmed by their oxidation to d- and l-*pinononic acid* (III).

The difficulty of preparing the verbenols by the autoxidation of α-pinene was also remarked upon by Wienhaus and Schumm,‡ but Blumann and Schmidt§ have found that *d*-verbenol can be conveniently prepared from *d*-verbenone by Ponndorf's method.‖ When the ketone is heated with aluminium *iso*propoxide in *iso*propyl alcoholic solution an alcohol is obtained, which, after purification through the benzoate, melts at about 8°, b.p. 95°/10 mm., $d^{15°}$ 0·9745, $n_D^{15°}$ 1·4938, $[\alpha]_D$ $+124°$. This *d*-verbenol is not, however, homogeneous, and evidently consists of a mixture of the two possible stereoisomeric forms, since, when

---

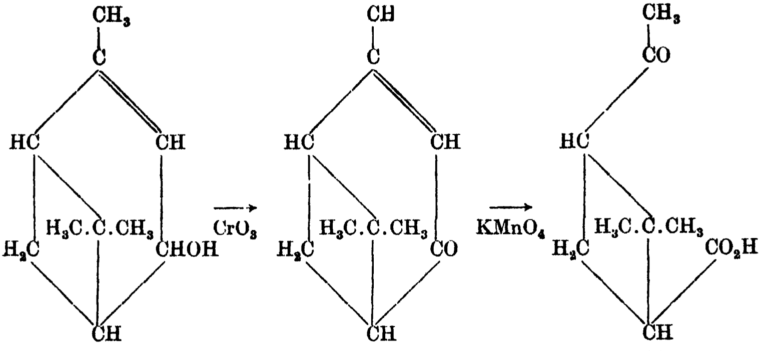
* *Annalen*, 1930, **478**, 303.

† *Ber.* 1913, **46**, 1194.

‡ *Annalen*, 1924, **439**, 20.

§ *Ibid.* 1927, **453**, 48.

‖ *Z. angew. Chem.* 1926, **39**, 138.



(I) (II) (III)

digested with acetic anhydride, it gives a mixture of *d*-verbenene (see below) and *d*-verbenol.

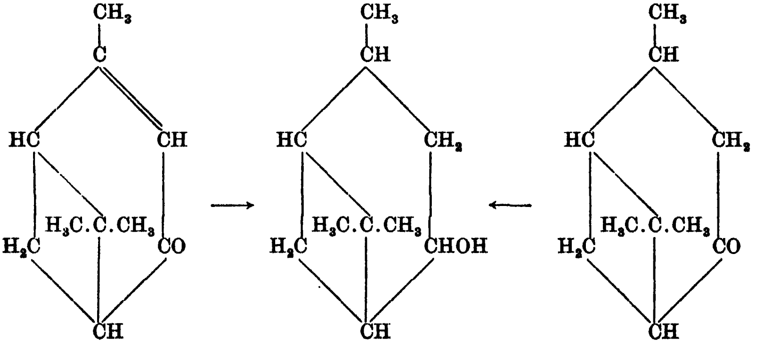
It is only recently that Schmidt, Schulz and Doll[*] have succeeded in separating each of the possible isomers in the pure state. From the autoxidation products of α-pinene they isolated a p-*nitrobenzoate*, m.p. 81–82°, $[\alpha]_D$ +156°, from which a *d*-verbenol, m.p. 20·6°, b.p. 92°/10 mm., $d^{20°}$ 0·9697, $n_D^{20°}$ 1·4916, $[\alpha]_D$ +144°, was obtained on saponification. A somewhat purer form of this isomer, having m.p. 24°, $[\alpha]_D$ +168°, was subsequently derived[†] from the products of the reduction of verbenone by the Ponndorf method. It was separated as its *p*-nitrobenzoate, and from the mother liquors there was then obtained a stereoisomeric d-*verbenol*, m.p. 15·5°, b.p. 90°/10 mm., $d^{20°}$ 0·9724, $n_D^{20°}$ 1·4932, $[\alpha]_D$ +65°. As would be anticipated, both stereoisomers gave the same *d*-verbenone on oxidation with chromic acid. On the basis of the Auwers-Skita rule, the alcohol, m.p. 24°, which has the lower density and refractive index, is probably the *trans*-isomer, and this is supported by its greater rate of esterification with *p*-nitrobenzoyl chloride; it is more stable towards dehydration than the *cis*-isomer. The reactions now to be described refer to the usual mixture of stereoisomers.

On catalytic hydrogenation in the presence of palladium crude *d*-verbenol was found by Wienhaus and Schumm to give d-*verbanol* (IV), b.p. 102°/20 mm., $d^{20°}$ 0·940, $n_D^{20°}$ 1·4761, which was a mixture of isomerides, but from which a crystalline

---

[*] *Schimmel's Report*, 1940, p. 38; *Chem. Zentr.* 1940, II, 3037.
[†] Schulz and Doll, *ibid.* 1944, II, 755.

hydrogen phthalate, m.p. 127°, could be prepared. Verbanol, as is the case with pinocampheol (p. 207), should theoretically exist in twelve possible forms (eight optically active, and four racemic), but few have as yet been isolated in the pure state. One of them may be obtained as a solid, m.p. 58°, b.p. 218°, $[\alpha]_D$ +1·3° (in alcohol), by the reduction of *d*-verbenone (II) with sodium in moist ether.[*] Kahnemann,[†] by the hydrogenation of verbanone (V) over platinum, has obtained a d-cis-*verbanol*, m.p. 74–75°, $[\alpha]_D$ +5·1° (*hydrogen phthalate*, m.p. 142–143°); by carrying out the reduction with sodium and alcohol he obtained a d-trans-*verbanol*, m.p. 69–70°, $[\alpha]_D$ +11·7° (*hydrogen phthalate*, m.p. 163–164°). Schulz and Doll, by hydrogenation of *trans*-verbenol, have obtained an isomer which they term iso*verbanol*, m.p. 76°, $[\alpha]_D$ +16° in benzene, which gives a p-*nitrobenzoate*, m.p. 95°, and a *hydrogen phthalate*, m.p. 190–191°. Similarly, from *cis*-verbenol, they have obtained neoiso*verbanol*, m.p. 74°, $[\alpha]_D$ +5° in benzene (p-*nitrobenzoate*, m.p. 135°; *hydrogen phthalate*, m.p. 142°), which is presumably identical with the *d*-*cis*-verbanol of Kahnemann.



(II) (IV) (V)

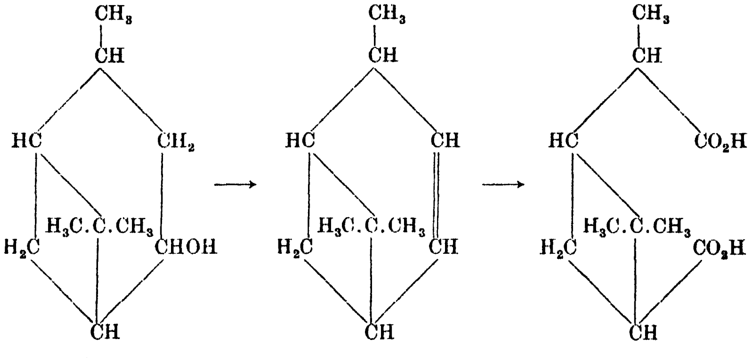
When *methyl verbanylxanthate*, b.p. 100–110°/23 mm., is distilled at the ordinary pressure it yields a hydrocarbon, b.p. 156–157°/758 mm., $d^{20°}$ 0·8604, $n_D^{20°}$ 1·4667, $[\alpha]_D$ −6·22°, which is probably *l*-δ-pinene (VI)[‡], since it gives no pinonic acid on oxidation. *dl*-δ-Pinene, b.p. 157–159°, $d_{4°}^{20°}$ 0·8636, $n_D^{20°}$ 1·4656, which gives dl-*pinocamphoric acid* (VII), m.p. 185–186°, on oxidation with permanganate, has been obtained* by the dehydration of *dl*-verbanol with thionyl chloride and pyridine.

---

[*] Blumann and Zeitschel, *Ber.* 1913, **46**, 1192.

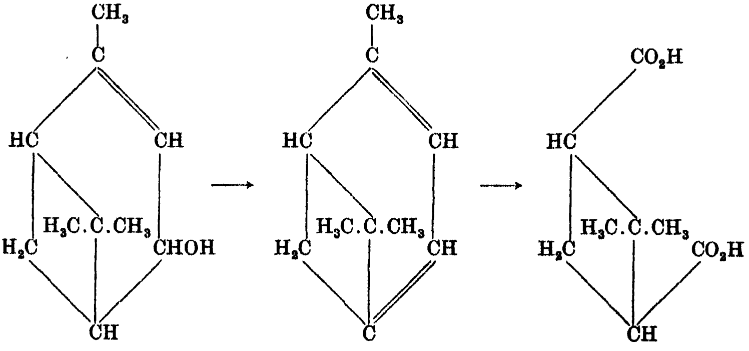
[†] *Bull. Soc. chim.* 1933 [iv], **53**, 1167.

[‡] Compare footnote **, p. 104.



(IV) (VI) (VII)

Results of considerable interest have been obtained by the investigation of the dehydration products of *d*-verbenol. With phosphorus pentoxide or zinc chloride *d*-verbenol yields *p*-cymene, but when boiled with acetic anhydride a hydrocarbon, l-*verbenene*, $C_{10}H_{14}$, b.p. 159–160°/758 mm., $d^{20°}$ 0·8822, $n_D^{20°}$ 1·4985, $[\alpha]_D$ – 74·90°, is obtained. Blumann and Zeitschel, who prepared this hydrocarbon,† considered it to have formula (VIII), which, if correct, would be contrary to the well-established Bredt rule.



(I) (VIII) (IX)

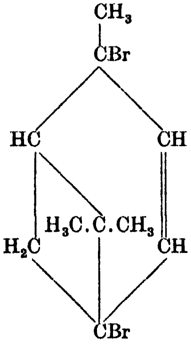
---

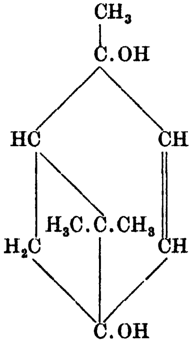
* Komppa and Klami, *Ber.* 1937, 70, 788.

† *Ber.* 1921, 54, 887.

They based this formula essentially on the following grounds: (i) oxidation yields *norpinic acid* (IX) which proved that the hydrocarbon must contain the *cyclo*butane ring, (ii) on bromination only a *dibromide* is formed, indicating a conjugated system of ethylenic linkages, and (iii) on reduction with sodium and alcohol only two atoms of hydrogen are taken up.

To the *dibromide*,* *d*- and *l*-forms, m.p. 70–72°, $[\alpha]_D$ +297·65°, −298·50° (in benzene), *dl*-, m.p. 50–52°, the formula (X) was assigned. This bromide on reduction with zinc dust in acetic acid solution was reconverted into the parent hydrocarbon, whilst with alkali a *glycol*, $C_{10}H_{16}O_2$ (XI), m.p. 141°, was obtained. As will be seen from the sequel, it is very unlikely that these formulae are correct.


(X)

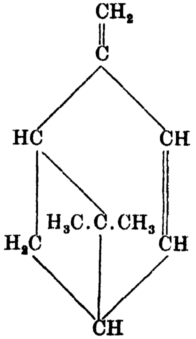

(XI)

Blumann and Zeitschel suggested that the hydrocarbon, *dihydroverbenene*, $C_{10}H_{16}$, b.p. 158–159°/762 mm., $d^{20°}$ 0·8625, $n_D^{20°}$ 1·4662, $[\alpha]_D$ +36·52°, obtained on reduction of verbenene, is δ-pinene (VI), in which case it would be identical with the hydrocarbon prepared by Wienhaus and Schumm from verbanol (p. 216). Blumann and Zeitschel attempted to confirm this constitution by oxidation of the hydrocarbon to *pinocamphoric acid* (VII), but in this they were unsuccessful, nor could they find any pinonic acid amongst the oxidation products. With hydrogen chloride *bornyl chloride* was obtained, with amyl nitrite *pinene nitrosochloride*, and with dilute sulphuric acid cis-*terpin hydrate*.

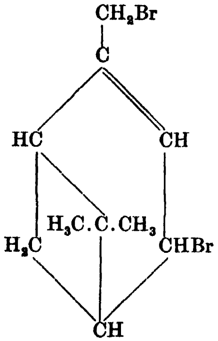
---

* The rotation of dibromide is opposite in sign to that of the hydrocarbon from which it is prepared.

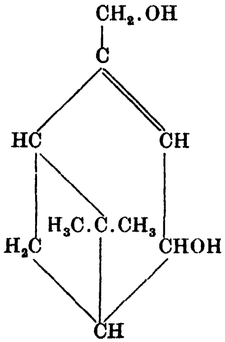
The formation of pinene nitrosochloride and *cis*-terpin hydrate shows that dihydroverbenene must contain some α-pinene, and Ruzicka and Trebler* suggest that verbenene is much more probably the β-pinene derivative (XII). This formula, whilst not in contradiction to the Bredt rule, accounts satisfactorily for all the reactions observed by Blumann and Zeitschel, and explains more readily the formation of norpinic acid on oxidation, the production of which, from a substance of formula (VIII), is difficult to interpret. A hydrocarbon of formula (XII) should give α-pinene on reduction and not δ-pinene. It may therefore be concluded, with a reasonable degree of certainty, that verbenene has the formula (XII); for the dibromide and glycol (XIII) and (XIV) are possible representations.



(XII)

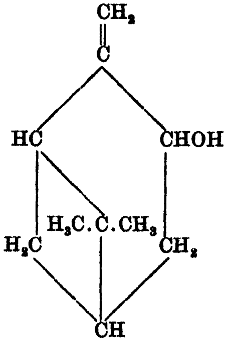


(XIII)



(XIV)

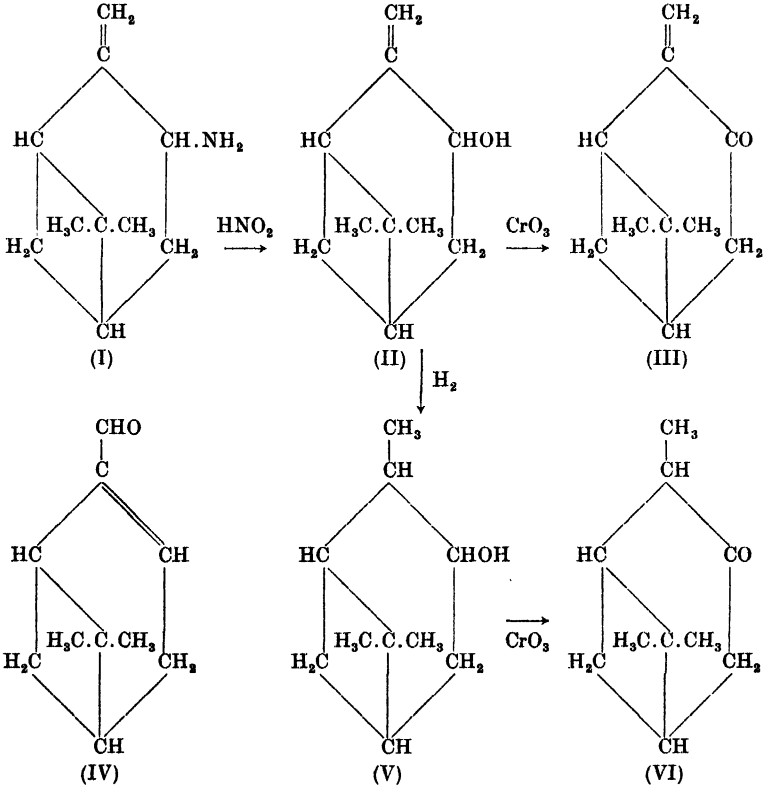
PINOCARVEOL



---

* *Helv. Chim. Acta*, **1924, 7, 489.**

In 1905 Wallach[*] separated from the high boiling fraction of the essential oil derived from *Eucalyptus globulus* a laevorotatory alcohol, $C_{10}H_{16}O$, identical apparently in structure with the substance which he had prepared many years previously[†] by the action of nitrous acid on *pinylamine* (I), and formulated as *pinocarveol* (II). When oxidised with chromic acid it gave a product which was thought to be pinocarvone (III), but which is now known to be a mixture of this ketone with myrtenal (IV), since the alcoholic portion of the oil contains both myrtenol and pinocarveol.[‡] A similar mixture is obtained by the autoxidation



---

[*] *Annalen*, 1906, **346**, 229. [†] *Ibid.* 1893, **277**, 149.

[‡] Schmidt, *Schimmel's Report*, 1941, p. 56. *Chem. Zentr.* 1942, I, 2530. Comment has already been made (p. 185) on the repercussions of this error on the chemistry of nitrosopinene and the confusion which thereby arose over the identities of myrtenol, pinocarvone and "carvopinone".

of β-pinene, and probably also by the oxidation of this hydrocarbon with selenium dioxide (see p. 199).

Even pure pinocarveol does not give a good yield of pinocarvone on oxidation, but the structure assigned to the alcohol is confirmed by its reduction to pinocampheol (V) which may be identified by oxidation to *pinocamphone* (VI).

Pinocarveol may be separated and purified through its borate, hydrogen phthalate, *p*-nitrobenzoate or phenylurethane. For the *dl*-form, the following constants have been recorded: b.p. 215–218°, 100–102°/12 mm., $d^{18°}$ 0·980, $n_D^{18°}$ 1·4988; the *d*-form, prepared by the autoxidation of β-pinene, has $[\alpha]_D$ +59°. According to Schmidt[*] the natural alcohol is the *l-trans*-form, and has m.p. 5°, b.p. 209–210°, $d^{20°}$ 0·981, $n_D^{20°}$ 1·5005, $[\alpha]_D$ −72° (*hydrogen phthalate*, m.p. 116–117°, $[\alpha]_D$ −65° (in alcohol); p-*nitrobenzoate*, m.p. 91–92°, $[\alpha]_D$ −40° (in benzene); *phenylurethane*, m.p. 88–89°; α-*naphthylurethane*, m.p. 95°). When shaken with dilute sulphuric acid it forms a *hydrate*, m.p. 196°. By the reduction of *l*-pinocarvone with aluminium *iso*propoxide, or by treatment of pinocarvone dibromide with zinc and acetic acid, there is obtained d-cis-*pinocarveol*, m.p. 51°, b.p. 217–218°, $d^{20°}$ 1·004, $n_D^{20°}$ 1·5057, $[\alpha]_D$ +55° (in alcohol) (p-*nitrobenzoate*, m.p. 104°, $[\alpha]_D$ +136° in benzene), which, unlike the *trans*-alcohol, undergoes dehydration on shaking with dilute sulphuric acid to give a *hydrocarbon*, b.p. 48–50°/8 mm., $[\alpha]_D$ +30°. The configurations are based on the Auwers-Skita rule and are supported by the greater rate of saponification shown by the *p*-nitrobenzoate of the *trans*-alcohol. The oxidation of either isomer with chromic acid gives pinocarvone, whilst, with potassium permanganate, pinic acid is obtained, thus confirming the presence of the *cyclo*butane ring. *l-cis*-Pinocarveol is converted into *d*-pinocamphone when distilled over copper at 280°,[†] treated with sodium,[‡] or heated to 170° with aluminium *iso*propoxide.[§]

With bromine in chloroform, *l-cis*-pinocarveol reacts in a remarkable manner, yielding a bimolecular *bromide*, $(C_{10}H_{16}OBr)_2$, m.p. 160°, which is stable to potassium permanganate;[‖] the *trans*-alcohol gives a non-crystalline product.

---

[*] *Ber.* 1944, 77, 167.

[†] Treibs and Schmidt, *Ber.* 1927, 60, 2340.

[‡] Schmidt, *Ber.* 1944, 77, 171.

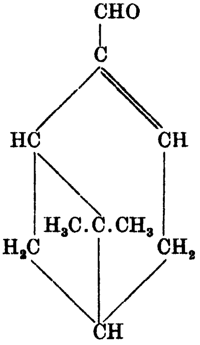
[§] *Idem, ibid.* 1929, 62, 103.

[‖] *Idem, ibid.* 1929, 62, 2948.

Unlike verbenol, pinocarveol can be readily acetylated; the cis-*acetate* has b.p. 231–232°, $d^{15°}$ 1·003, $n_D^{20°}$ 1·4802, $[\alpha]_D + 64°$, and the trans-*acetate* has b.p. 227–228°, $d^{15°}$ 0·999, $n_D^{20°}$ 1·4772, $[\alpha]_D + 16°$.

C. ALDEHYDE

MYRTENAL



The unsaturated aldehyde, *d*-myrtenal, $C_{10}H_{14}O$, was found by Semmler and Zaar* to occur in the oil known as false camphor wood oil, which is probably derived from the wood of *Hernandia peltata* Meissn., but the aldehyde had been prepared previously by Semmler and Bartelt† by the oxidation of the primary alcohol, *d*-myrtenol (see p. 211). *d*-Myrtenal occurs in the wood oil associated with the monocyclic aldehyde, perillaldehyde (Vol. I, p. 311) and, although it can be partially separated from this by fractional distillation, the separation is most readily effected by treating the mixture with neutral sodium sulphite solution. Both the aldehydes combine with this reagent but, by the action of alkali, only *d*-myrtenal is regenerated. It has recently been found by Schmidt‡ that the aldehyde also occurs in the oil from *Eucalyptus globulus*.

Dupont, Zacharewicz and Dulou§ have shown that myrtenal, and not verbenone, is the main product formed by the oxidation of α-pinene with selenium dioxide. Furthermore, Schmidt[*] has proved that the substance formerly described as "pinocarvone" obtained from β-pinene either by autoxidation or by treatment with selenium dioxide, is largely composed of myrtenal. Since it has also been established that the alcoholic portion of the oil from *E. globulus* is not, as hitherto supposed, pure pinocarveol, but a mixture of this alcohol with myrtenol (I), it follows that the "pinocarvone" obtained on oxidation of this material likewise contains a considerable proportion of the aldehyde. The presence of myrtenal (II) in these products is established by conversion, either directly, or through the *oxime* (III) and *nitrile* (IV) into crystalline *myrtenic acid* (V).

---

* *Ber.* 1911, **44**, 815.

† *Ibid.* 1907, **40**, 1366.

‡ *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530.

§ *Compt. rend.* 1934, **198**, 1699; *Bull. Soc. chim.* 1935 [v], **2**, 533.

The constitution of the aldehyde (II) follows from its preparation by the oxidation of *d*-myrtenol (I) with chromic acid; the evidence on which the constitution of the latter is based has been discussed on p. 210.

For the aldehyde prepared from the wood oil, Semmler and Zaar gave the following values: b.p. 89–92°/11 mm., d^{20° 0·9859, n_D 1·5061, $[\alpha]_D$ +13·6°, whilst for a specimen prepared by the oxidation of *d*-myrtenol with chromic acid and purified through the semicarbazone Rupe and Héritier[†] recorded: b.p. 91·75°/12·5 mm., $d_{4^\circ}^{20^\circ}$ 0·9898, $[\alpha]_D$ +15·6°. Very similar constants, b.p. 220–221°, d^{15° 0·991, $n_D^{20^\circ}$ 1·5030, $[\alpha]_D$ +13°, have been given by Schmidt for the aldehyde isolated from *E. globulus*, whilst l-*myrtenal*, obtained by the autoxidation of β-pinene, has b.p. 220–221°, d^{20° 0·992, $n_D^{20^\circ}$ 1·5028, $[\alpha]_D$ −15°. These figures, and also those for the derivatives described below, are in excellent agreement with the constants given in the earlier literature for "pinocarvone".[‡] The aldehyde shows the very considerable molecular exaltation of 1·19 units. This is obviously occasioned by the conjugation of the aldehyde group with the ethylenic linkage.

On hydrogenation over a palladium-charcoal catalyst,[§] myrtenal gives *dihydromyrtenal* (myrtanal) (VI), b.p. 75–76°/2·5 mm.,

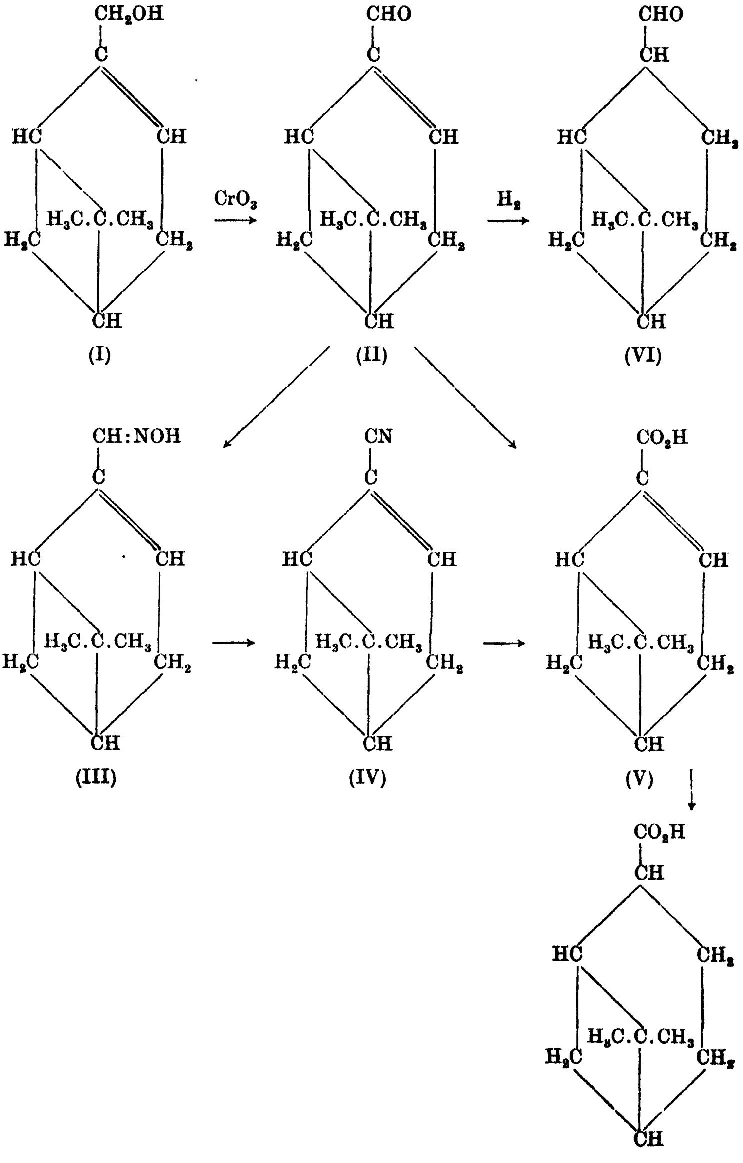
---

[*] *Loc. cit.*

[†] *Annalen*, 1927, **459**, 189.

[‡] Compare, *inter al.*, Auwers and Eisenlohr, *J. pr. Chem.* 1910 [ii], **82**, 138; Schmidt, *Ber.* 1930, **63**, 1131; Stallcup and Hawkins, *J. Amer. C.S.* 1941, **63**, 3339; 1942, **64**, 1807.

[§] Schmidt, *Schimmel's Report*, 1941, p. 70; *Chem. Zentr.* 1942, I, 2531; Dupont, Zacharewicz and Dulou, *loc. cit.*


(I)
CrO_3
(II)
H_2
(VI)
(III)
(IV)
(V)
(VII)

$d^{15°}$ 0·974; $n_D^{20°}$ 1·4802; the *l*-form shows $[\alpha]_D$ −37°. If a platinum catalyst is used* dihydromyrtenol (p. 212) is obtained.

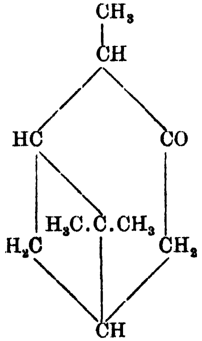
Oxidation of *d*- or *l*-myrtenal gives myrtenic acid (V), m.p. 53–54°.

Myrtenal can be characterised by the preparation of the *semicarbazone* (*d*- and *l*-, m.p. 220°; *dl*-, m.p. 206°), the *phenylsemicarbazone* (*d*-, m.p. 180°), the 2:4-*dinitrophenylhydrazone* (*l*-, m.p. 223°), or the *oxime* (*d*-, m.p. 71–72°, b.p. 125–128°/9 mm., $d^{20°}$ 1·029, n_D 1·5380, $[\alpha]_D$ +42°; *l*-, m.p. 69–70°; *dl*-, m.p. 98°). Digestion of the *d*-oxime (III) with acetic anhydride gives the *nitrile* (IV), from which by hydrolysis d-*myrtenic acid*, $C_{10}H_{14}O_2$ (V), m.p. 54°, b.p. 148°/9 mm., can be prepared.† This acid, on reduction with sodium and alcohol, gives *dihydromyrtenic acid*, $C_{10}H_{16}O_2$ (VII), b.p. 142–144°/8 mm., $d^{20°}$ 1·049, n_D 1·4857.

Attention has already been directed (Vol. I, p. 312) to the biogenetic interest attaching to the association of myrtenal, perillaldehyde, limonene and α-pinene in the false camphor wood oil.

D. KETONES

PINOCAMPHONE



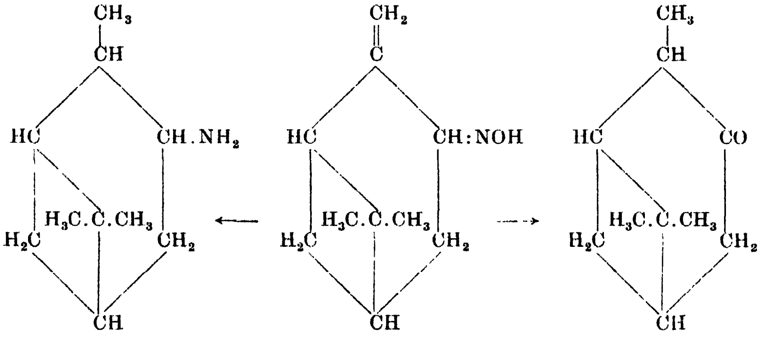
l-Pinocamphone, $C_{10}H_{16}O$, occurs in oil of hyssop, which is obtained from the herb *Hyssopus officinalis*, being present in this oil to the extent of approximately 45 per cent. Although the natural occurrence of the ketone was first observed by Schimmel and Co.,* the *dl*-form had been prepared many years previously by Wallach† by the reduction of *nitrosopinene* (I) with zinc dust in acetic acid solution. As has been mentioned (p. 182), the main product of the reduction is the base *pinylamine* (II), but a considerable quantity (22 per cent.) of the saturated ketone (III) is formed also. The dextrorotatory ketone does not occur in nature, but it has been prepared from *l*-pinocarveol (see below).

---

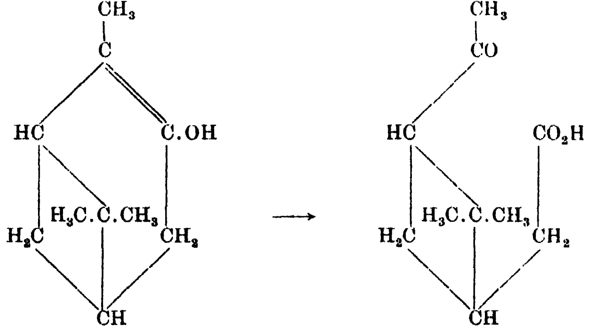
* Dupont and Zacharewicz, *Compt. rend.* 1934, **199**, 365.

† A similar series of reactions on the *l*-aldehyde has been carried out by Schmidt (*Schimmel's Report*, 1941, p. 70).

The constitution of *dl*-pinocamphone was determined by Wallach, who showed that, on oxidation with either potassium permanganate or chromic acid, dl-*pinonic acid* (VI) and dl-*pinocamphoric acid* (VII), m.p. 186–187°, were obtained. These



(II) (I) (III)

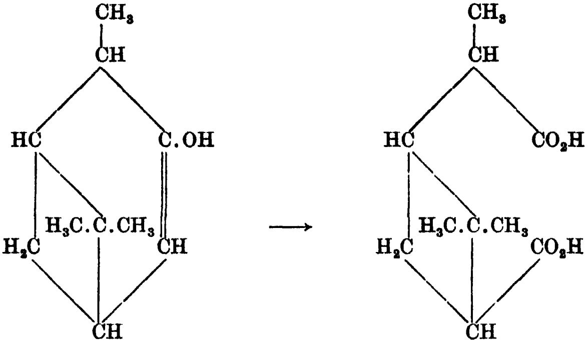


(IV) (VI)

---

* *Schimmel's Report,* 1908, April, p. 58; 1909, Oct., p. 69; Gildemeister and Köhler, *Wallach Festschrift,* 1909, p. 414.

† *Annalen,* 1892, **268**, 210; 1898, **300**, 287; 1900, **313**, 367; 1906, **346**, 235; 1908, **360**, 92.



(V) (VII)

acids result from the degradation of the two *enolic* forms (IV) and (V) of the ketone.

Gildemeister and Köhler have found *l*-pinocamphone to behave similarly, yielding a mixture of l-*pinonic acid* and l-*pinocamphoric acid*, m.p. 189–190°.

The constitution assigned to pinocamphone has been confirmed by its partial synthesis from ethyl *dl*-pinonate by Ruzicka and Trebler,* an outline of the method having already been given (p. 130). Recently, the ketone has been synthesised by Komppa, Klami and Kuvaja† from verbanone (VIII), which was treated with sodamide and carbon dioxide to give the *acid* (IX), and then reduced electrolytically to the *hydroxy-acid* (X), m.p. 144–145°. On dehydration with acetic anhydride this gave a d-δ-*pinene-2-carboxylic acid* (XI), m.p. 123°, $[\alpha]_D$ +10·6° (in chloroform), the acid chloride of which, by reaction with sodium azide, gave *l*-pinocamphone (*semicarbazone*, m.p. 226–228°). Since verbanone has been obtained synthetically, this amounts to a total synthesis of pinocamphone.

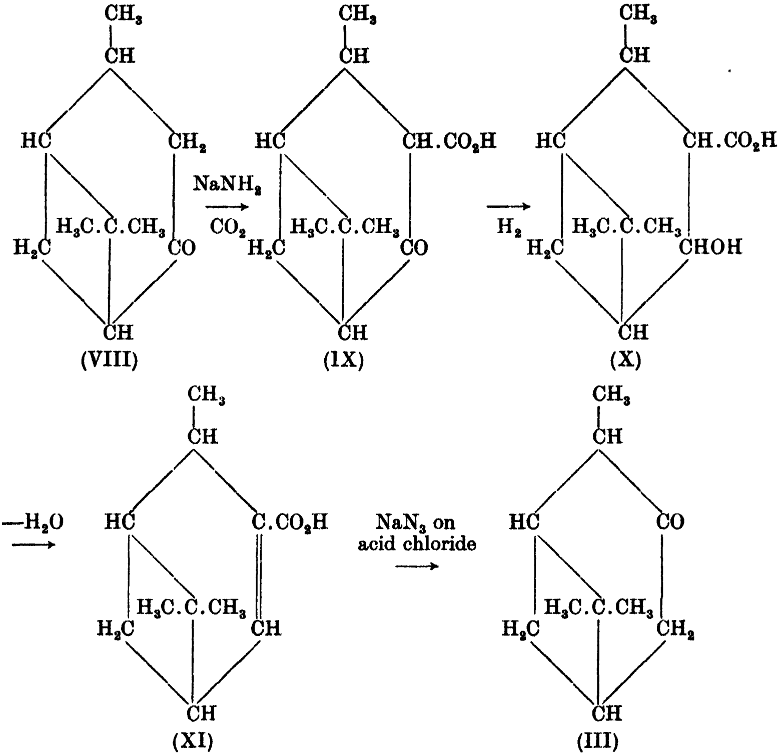
Pinocamphone can be most conveniently identified either by oxidation to pinonic acid or by the preparation of the *semicarbazone*. The recorded melting points of the latter derivative, however, are widely divergent, probably owing to the existence of the parent ketone in stereoisomeric modifications (see p. 230).

Pinocamphone is an oil with an odour reminiscent both of camphor and thujone. For the active ketone the following

---

* *Helv. Chim. Acta*, 1921, **4**, 666.

† *Annalen*, 1941, **547**, 185.

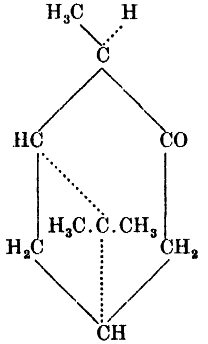


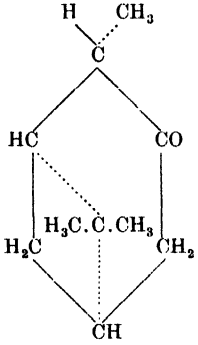
constants were observed: b.p. 212–213°/765 mm., d^{15° 0·9662, $n_D^{20^\circ}$ 1·4742, $[\alpha]_D$ $-13{\cdot}42^\circ$; whilst for the ketone prepared from nitrosopinene Wallach and Engelbrecht[*] give b.p. 211–213°, 87°/12 mm., d^{21° 0·959, $n_D^{21^\circ}$ 1·4727.

Pinocamphone can exist in two stereoisomeric modifications, represented by formulae (III a) and III b). Following the nomenclature adopted in the menthone series (Vol. I, p. 234), the former, having a *trans*-configuration of the methyl group with respect to the *gem*-dimethyl bridge, is termed *pinocamphone*, whilst the isomer is named iso*pinocamphone*. Treatment of either stereoisomer with sodium ethoxide or alcoholic hydrogen chloride results in the formation of an equilibrium mixture of the *cis*- and *trans*- forms, though, in contrast to the inversion shown by menthone, there is no change in the sign of optical rotation. The pure stereoisomerides can be prepared by oxidation of the appropriate pinocampheols (p. 207) with chromic acid. It is noteworthy, however, that although *d*-pinocamphone is obtained by oxidation of *d*-pinocampheol, *d*-*iso*pinocamphone is formed by the oxidation of *l*-*iso*pinocampheol.

---

[*] *Annalen*, 1906, **346**, 236.


(IIIa)


(IIIb)

The formulae are assigned on the basis of the Auwers-Skita rule, according to which the *cis*-ketone possesses the higher density and refractive index. These conclusions are also supported by experiments on the formation of oximes, the rate of reaction being greater for pinocamphone than for *iso*pinocamphone. The properties of the ketones are summarised in the following table:*

					M.p. of derivatives	
Pinocamphone	B.p.	$d^{15°}$	$n_D^{20°}$	α_D	Semicarbazone	Oxime
d- and *l*-	211°	0·964	1·4728	±23°	227°	56°
dl-	—	—	—	± 0°	208°	89°
d- and *l*-*iso*-	212°	0·969	1·4748	±10·5°	219°	Liq.
dl-*iso*-	—	—	—	± 0°	—	88°

Although the melting-points of the *dl*-oximes are almost identical, the mixed melting-point is depressed to 65°. Schmidt has shown that the *dl*-*cis*-oxime is identical with that described by Wallach† from the *dl*-ketone which he had obtained by the reduction of nitrosopinene with zinc dust, whereas the *dl*-*trans*-

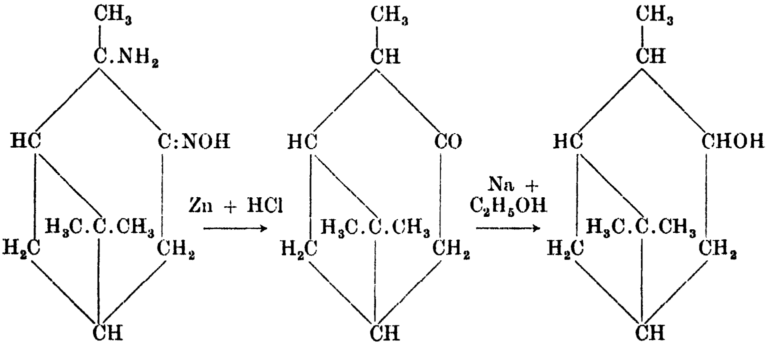
---

* Schmidt, *Schimmel's Report*, 1934, p. 99; 1941, p. 50; *Ber.* 1944, **77**, 544. According to Delépine and Badoche, however, the *d*- and *l*-*trans*-semicarbazones have m.p. 265°, and the *d*- and *l*-*cis*, m.p. 282°. They also quote a higher m.p., 65°, for the *d*-*trans*-oxime (*Ann. Chim.* 1948 [xii], **3**, 573).

† *Annalen*, 1898, **300**, 287.

oxime is identical with that prepared by Wallach and Ost[*] by the direct catalytic hydrogenation of nitrosopinene.

Pinocamphone has also been obtained by the hydrogenation of pinocarvone (p. 240)[†] and by the distillation of pinocarveol (p. 222) over copper in a current of hydrogen at 280°.[‡] According to Schmidt[§] a *d*-pinocamphone, b.p. 207°/756 mm., d^{20° 0·9572, $[\alpha]_D$ +14·2° is formed when *l*-pinocarveol is heated with aluminium *iso*propoxide at 170°. *dl*-Pinocamphone was also prepared by Leach[||] by the reduction of *pinene nitrolamine* (XII) with zinc in alcoholic hydrochloric acid solution. Reference has been made on p. 146 to the preparation of the ketone from hydroxypinocamphone.



(XII) (III) (XIII)

On reduction with sodium and alcohol pinocamphone gives the corresponding secondary alcohol, *pinocampheol* (XIII),[¶] the *cis*-ketone, however, giving a *trans*-alcohol.

In acetic acid pinocamphone can be readily brominated to give a *dibromide*,[**] the *dl*- form of which melts at 118–119°[††] and the *l*-form at 93–94°, $[\alpha]_D$ −49·24° (in ether). The position of the bromine atoms has not been determined.

---

[*] *Annalen*, 1912, **389**, 185.

[†] Schmidt, *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530. The product obtained by Stallcup and Hawkins (*J. Amer. C.S.* 1942, **64**, 1807) was probably dihydromyrtenal, since their "pinocarvone" was mainly myrtenal (see p. 224).

[‡] Treibs and Schmidt, *Ber.* 1927, **60**, 2340.

[§] *Ibid.* 1929, **62**, 103.

[||] *J.C.S.* 1907, **91**, 9.

[¶] Wallach, *Annalen*, 1898, **300**, 288; Schmidt, *Schimmel's Report*, 1934, p. 97; Gildemeister and Köhler, *Wallach Festschrift*, 1909, p. 414.

[**] Schmidt, *Schimmel's Report*, 1941, p. 50.

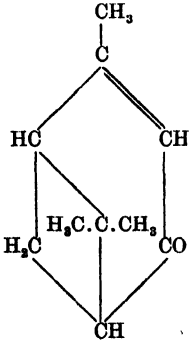
[††] Wallach and Engelbrecht, *Annalen*, 1906, **346**, 236.

By the reduction of *dl*-pinocamphoneoxime with sodium and alcohol, dl-*pinocamphylamine*, b.p. 198–199°, is obtainable.[*] This base is formed also by the reduction of nitrosopinene with sodium in amyl alcoholic solutions[†] and by the catalytic hydrogenation of pinylamine.[‡] Pinocamphylamine can be characterised by the preparation of *pinocamphylcarbamide*, m.p. 204°. The preparation of α- and δ-pinenes from the trimethylammonium hydroxide derivative has already been referred to on p. 130. When pinocamphoneoxime is treated with sulphuric acid or with phosphorus pentoxide, it yields the nitrile of a monobasic acid, *pinocampholenic acid*, $C_9H_{15}CO_2H$. This acid is an oil, *amide*, m.p. 116°, and its constitution has not been determined, but it is probably a *cyclo*pentane derivative.

dl-*Pinocamphonehydrazone*, b.p. 134–135°/22 mm., $d^{20°}$ 0·9917, $n_D^{20°}$ 1·5155, was prepared by Nametkin and Jarzev,[§] who converted it by the Kishner process into pinane.

According to Hugh and Kon[‖] pinocamphone cannot be condensed with the sodium derivatives of ethyl malonate, ethyl cyanoacetate or ethyl acetoacetate nor does it condense with ethyl bromoacetate in the presence of zinc. The action of methyl magnesium iodide on the ketone has been studied by Hasselström and von Konow.[¶]

VERBENONE



---

[*] Wallach, *Annalen*, 1900, **313**, 367.

[†] Tilden and Shepheard, *J.C.S.* 1906, **89**, 1561.

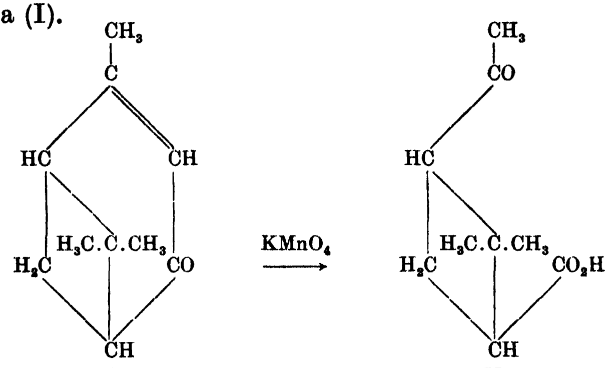
[‡] Ruzicka and Trebler, *Helv. Chim. Acta*, 1924, **7**, 489.

[§] *Ber*. 1923, **56**, 832.

[‖] *J.C.S.* 1927, p. 2600.

[¶] *Ann. Acad. Sci. Fennicae*, 1930, no. **11**, 3.

d-Verbenone, $C_{10}H_{14}O$, was found by Kerschbaum[*] to occur in Spanish verbena oil (from *Verbena triphylla* L.) to the extent of about 1 per cent. In this oil it occurs in association with citrals *a* and *b*, from which it can be separated by removal of the two aldehydes by condensation with cyanoacetic acid (Vol. I, p. 100). Owing to the limited quantity of material available, Kerschbaum was unable to subject the ketone to a detailed study, but since it gave d-*pinononic acid* (II), m.p. 128–129°, on oxidation with potassium permanganate, he suggested that it probably had formula (I).



(I) (II)

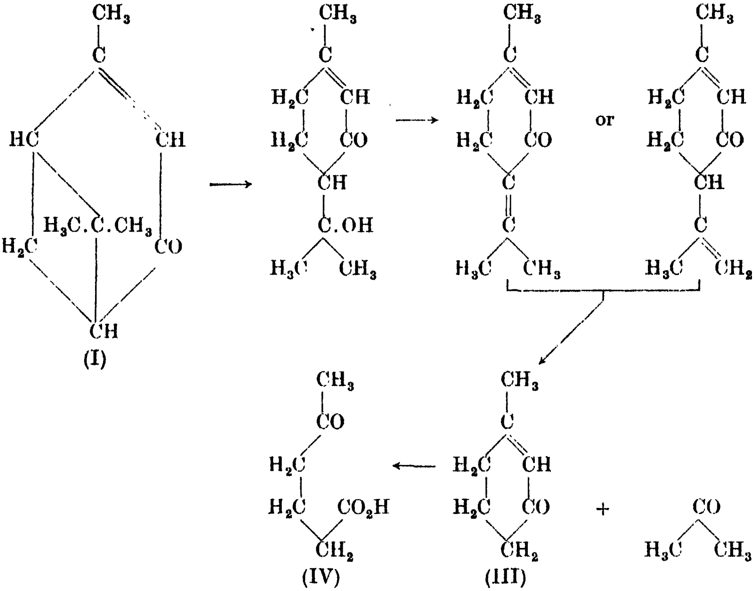
In 1913, Blumann and Zeitschel,[†] during an investigation of the products which are formed by the autoxidation of *d*-α-pinene, separated a ketone which had properties identical with those of Kerschbaum's *d*-verbenone. A careful study of the reactions of the ketone, together with those of the corresponding *l*-verbenone prepared by the autoxidation of *l*-α-pinene, confirmed the constitution assigned by Kerschbaum.

Oxidation of *d*- and *l*-verbenones gave *d*- and *l*-pinononic acids, whilst, when digested for some hours with dilute sulphuric acid, decomposition occurred with the formation of acetone and 1-*methyl*-Δ^1-cyclo*hexen*-3-*one* (III). The constitution of the latter, b.p. 200–202°/760 mm., *semicarbazone*, m.p. 198°, was proved by its oxidation to *γ-acetobutyric acid* (IV). This degradation of *d*-verbenone evidently proceeds in accordance with the following scheme, although it has not proved possible to isolate any of the intermediate products.

---

[*] *Ber.* 1900, 33, 885.

[†] *Ibid.* 1913, 46, 1178.



The conversion of *d*-verbenone into the monocyclic ketone, together with its oxidation to *d*-pinononic acid, leave no doubt that it has been correctly represented by (I).

Verbenone can be identified by the preparation of the *semicarbazone*, the *d*- and *l*-forms of which crystallise in leaflets, m.p. 208–209°, the *dl*-form melting at 180–181°.

The ketone is a colourless oil with an odour reminiscent both of camphor and peppermint; it rapidly becomes yellow on exposure to the air. For *d*-verbenone from verbena oil, which had been regenerated from the semicarbazone by hydrolysis with phthalic acid, Kerschbaum observed the following constants: b.p. 103–104°/16 mm., d^{17° 0·974, $n_D^{17^\circ}$ 1·4995, $[\alpha]_D$ +66°; whilst Blumann and Zeitschel found for the ketone prepared from *d*-α-pinene: m.p. 6·5°, b.p. 227–228°, 100°/16 mm., d^{20° 0·9780, $n_D^{18^\circ}$ 1·4992, $[\alpha]_D$ +249·62°. The authors directed attention to the remarkably high rotatory power of the ketone, and it is not improbable that 180° should be added to the value observed by Kerschbaum. An even purer specimen, m.p. 9·8°, $[\alpha]_D$ +273, $d_{4^\circ}^{20^\circ}$ 0·9754, $n_D^{20^\circ}$ 1·4965, has been obtained by Schulz and Doll[*]

---

[*] *Chem. Zentr.* 1944, II, 755.

after repeated crystallisation from petroleum. *l*-Verbenone has not been obtained pure, since the *l*-α-pinene used in its preparation contained some *dl*-pinene.

The autoxidation of α-pinene takes a considerable time and the yield of the ketone is poor. It can best be isolated by fractional distillation and treatment of the appropriate fraction (b.p. 105–107°/5 mm.) with semicarbazide, when verbenone semicarbazone readily crystallises. A somewhat less satisfactory process is to take advantage of the compound which it forms with sodium sulphite in neutral solution, but some loss occurs owing to the formation of stable sulphonates. The ketone can be regenerated from the sodium sulphite derivative by the action of sodium carbonate. Wienhaus and Schumm[*] found that α-pinene can be conveniently and rapidly oxidised by oxygen in the presence of colloidal osmium[†] or cobalt resinate, and the verbenones are therefore comparatively readily accessible. It is important to recognise, however, that the product may be contaminated with myrtenal, and rigorous purification is therefore necessary.[‡]

By the catalytic hydrogenation of *d*-verbenone, Wienhaus and Schumm prepared the saturated ketone, d-*verbanone* (V), which had been obtained previously by Blumann and Zeitschel by the oxidation of d-*dihydroverbenol* (see p. 237). This ketone, which is isomeric with pinocamphone (p. 226), has b.p. 222°/760 mm., $d^{20°}$ 0·961, $n_D^{20°}$ 1·4751, $[\alpha]_D$ +52·55°, and can be characterised by the preparation of the *semicarbazone*, m.p. 230°, and the *oxime*, m.p. 88°, though it has not been established whether these derivatives are related to the *cis*- or to the *trans*-ketone.[§]

The total synthesis of *dl*-verbanone has been achieved by Komppa and Klami.[||] Methyl pinononate (VI), the synthesis of which by Guha and Ganapathi[¶] has already been described (p.150), undergoes the Reformatsky reaction, with methyl bromoacetate and zinc, to give the hydroxy-ester (VII). Dehydration of this ester with thionyl chloride gives *dimethyl dehydro*iso*homo-*

---

[*] *Annalen*, 1924, **439**, 20.

[†] Compare Willstätter and Sonnenfeld, *Ber.* 1913, **46**, 2953; 1914, **47**, 2814.

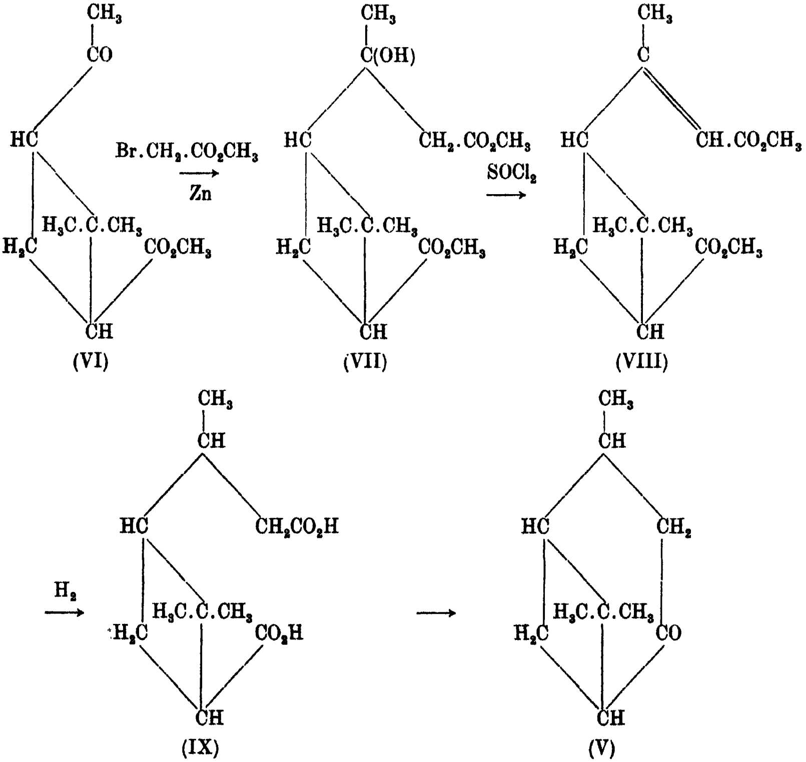
[‡] Dupont and Zacharewicz, *Compt. rend.* 1934, **198**, 1699; 1935, **200**, 759. These authors have also shown that, contrary to earlier reports, the oxidation of α-pinene with selenium dioxide gives, not verbenone, but myrtenal.

[§] Compare Schulz and Doll, *Chem. Zentr.* 1944, II, 755.

[||] *Ber.* 1937, **70**, 788.

[¶] *Ibid.* 1936, **69**, 1185.

pinocamphorate (VIII), the structure of which is proved by oxidation with potassium permanganate to *dl*-pinononic acid. The unsaturated dibasic acid, m.p. 194°, obtained by saponification of the ester (VIII) is hydrogenated over platinum to iso*homopinocamphoric acid* (IX), the lead salt of which, on heating, gives *dl*-verbanone (V), identified as its *semicarbazone*, m.p. 217°.



Verbanone shows a number of interesting reactions, and reference to some of these may be made here.

According to Guha and Rao* it is oxidised to verbenone by treatment with selenium dioxide.

Verbanone *hydrazone* (X), m.p. 27°, b.p. 146°/22 mm., gives *pinane* (XI) when heated with sodium ethoxide at 140–160°.

---

* *J. Ind. Inst. Sci.* **1939, 22A, 317.**

On hydration with dilute sulphuric acid or hydrochloric acid verbanone undergoes ring fission and yields Δ^1-o-*menthen*-3-*one* (XII), an analogous reaction occurring on reduction by Clemmensen's method, when o-*menthan*-3-*one* (XIII) is obtained. This fission of the *cyclo*butane ring in the pinane series to yield derivatives of *o*-menthane is apparently unique. Ring fission occurs also when verbanone is condensed with benzaldehyde in the presence of hydrogen chloride, a *dibenzylidene* derivative, m.p. 143°, being obtained, to which Wallach[*] assigned formula (XIV).

With *iso*amyl nitrite in the presence of sodamide verbanone reacts to yield an *oximino*-derivative (XV), m.p. 140°, which gives with acetic anhydride the *imide* of pinocamphoric acid (XVI).

By the reduction of *d*-verbenone with sodium in moist ethereal solution Blumann and Zeitschel[†] prepared the saturated secondary alcohol d-*dihydroverbenol* or *verbanol*, which is isomeric with pinocampheol. It can be obtained also by the reduction of verbenone with sodium in alcoholic solution, when it is accompanied by a *pinacone*, m.p. 211–212°. The properties of verbanol have already been discussed (p. 216).

On ozonolysis, verbenone gives pinononic acid, whilst with hydrogen peroxide in alkaline solution an *oxide* (XVII), m.p. 65°, b.p. 120–127°/24 mm., $d_{4^\circ}^{20^\circ}$ 1·0561, $n_D^{20^\circ}$ 1·4831, $[\alpha]_D \pm 102^\circ$, *semicarbazone*, m.p. 220°, is obtained. This latter reaction is general in the case of cyclic ketones containing an ethylenic linkage in the $\alpha:\beta$-position. When heated with methanolic potassium hydroxide, the oxide rearranges to 2-*hydroxyverbenone* (XVIII), m.p. 119–121° (*semicarbazone*, m.p. 191°),[‡] the reactions of which prove it to have this enol structure, since it shows no tendency to react in the diketo-form.

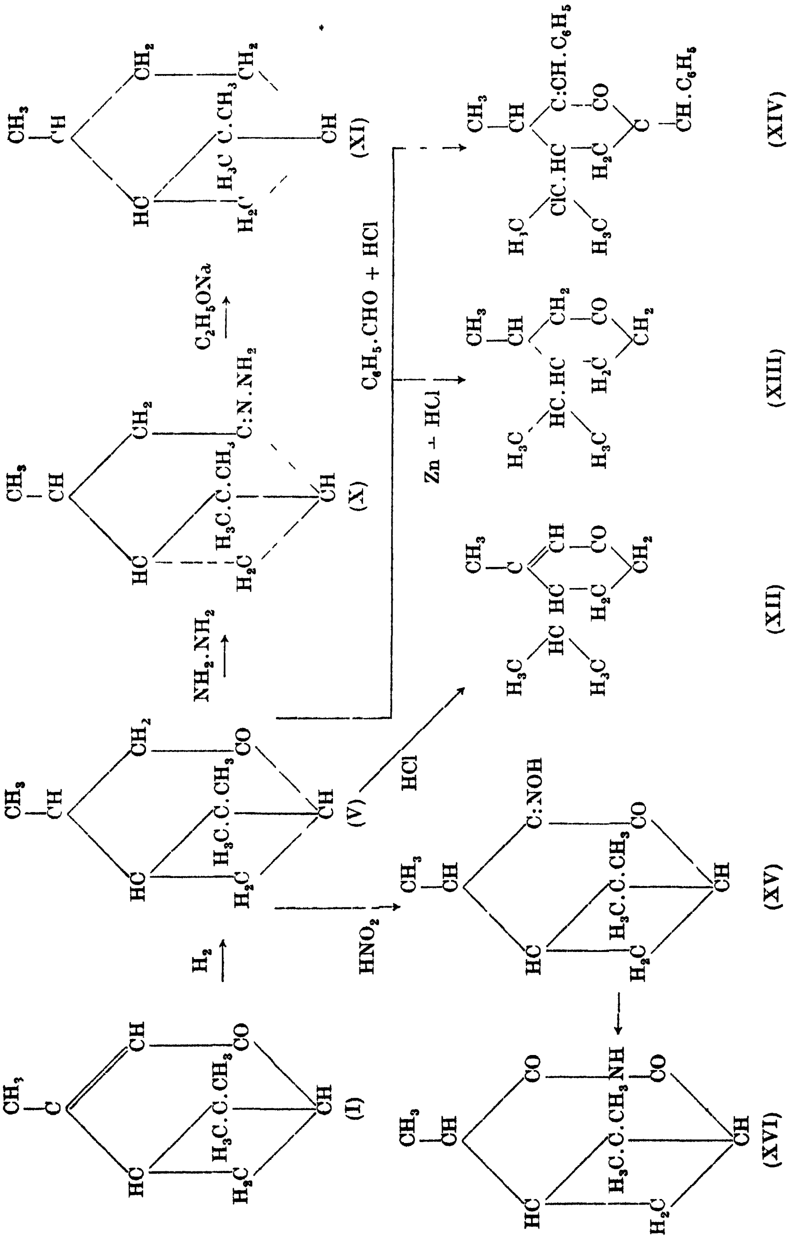
Kerschbaum observed that *d*-verbenone did not react with bromine in chloroform solution and it is similarly resistant to hydrogen chloride in carbon disulphide or ethereal solution. In acetic acid, however, addition of hydrogen chloride does occur accompanied by ring fission, but the halogenated *cyclo*hexanone derivative has not been obtained pure.

---

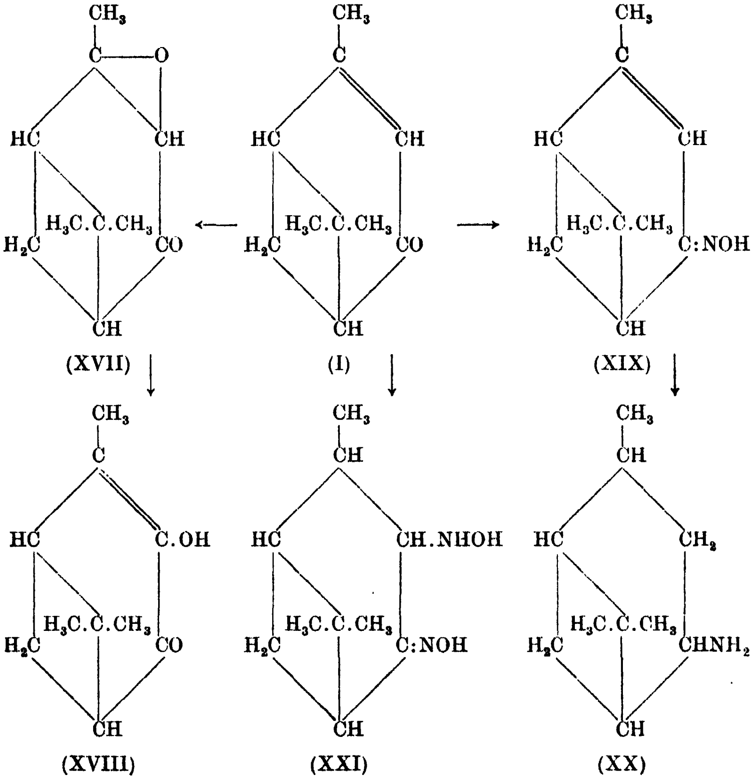
[*] *Annalen*, 1924, **437**, 188.

[†] *Ber.* 1913, **46**, 1192.

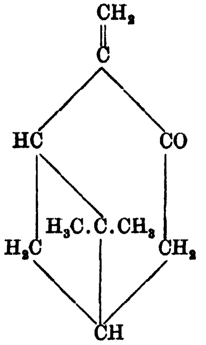
[‡] Treibs, *Ber.* 1933, **66**, 1491.


(I)
H_2
(V)
$NH_2.NH_2$
(X)
C_2H_5ONa
(XI)
$C_6H_5.CHO + HCl$
$Zn + HCl$
HCl
HNO_2
(XII)
(XIII)
(XIV)
(XV)
(XVI)

By the catalytic hydrogenation of d-*verbenoneoxime* (XIX), m.p. 119–120°, in the presence of palladium d-*verbanylamine* (XX), b.p. 211°/760 mm., $d_{4^\circ}^{20^\circ}$ 0·9184, $n_D^{20^\circ}$ 1·4812, is obtained. When *d*-verbenone is treated with an excess of hydroxylamine it gives a *hydroxylamino-oxime* (XXI) decomposing at 165°.



PINOCARVONE



Pinocarvone (I) has only recently been found to occur in nature, the *l*-form having been isolated by Schmidt* from the oil of *Eucalyptus globulus.*

Reports of the preparation of optically active and inactive pinocarvones have appeared in the literature since 1893, when Wallach† described a *dl*-pinocarvone which he had prepared from a substance believed to be *dl*-pinocarveol (II). Furthermore, *d*-pinocarvone was said to be formed by the autoxidation of β-pinene.‡ As already pointed out, however (pp. 183, 185, 199), it has now been established by Schmidt§ that these specimens of pinocarvone consisted mainly, if not entirely, of myrtenal. The effect of these errors, particularly on the problem of the constitution and reactions of nitrosopinene (see pp. 182, 185) was far-reaching, and it is only since 1941 that it has been possible to correlate and explain the results which have been recorded over a period of fifty years.

In 1906, Wallach‖ obtained an optically inactive oil, b.p. 95–96°/12 mm. (*semicarbazone*, m.p. above 300°), by the hydrolysis of nitrosopinene with oxalic acid. Since the product differed from his "dl-*pinocarvone*" it was named "*carvopinone*" and formulated as (IV). Schmidt has now shown that "carvopinone" is, in fact, the true *dl*-pinocarvone (I) the formation of which from nitrosopinene (III) does not involve any abnormal reaction. It follows that the "carvopinone" of Stallcup and Hawkins* obtained in small yield by the oxidation of β-pinene with selenium dioxide, is also *dl*-pinocarvone.†

---

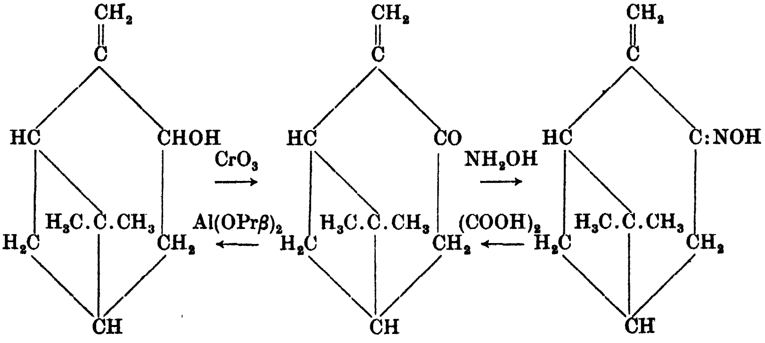
* *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530.

† *Annalen*, 1893, **277**, 150; 1894, **279**, 387; 1906, **346**, 222.

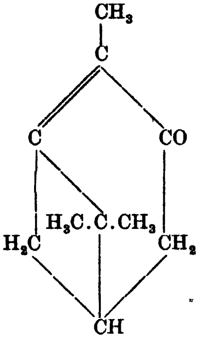
‡ Schmidt, *Ber.* 1930, **63**, 1130.

§ *Schimmel's Report*, 1941, p. 56; *Chem. Zentr.* 1942, I, 2530.

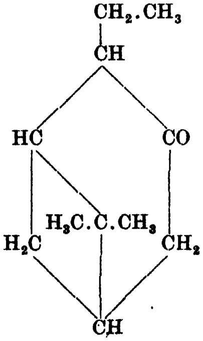
‖ *Annalen*, 1906, **346**, 232.



(II) (I) (III)



(IV)



(V)

Mention has already been made (p. 222) of the formation of pinocarvone in poor yield by the oxidation of pinocarveol (II).

Pinocarvone can be separated and purified by formation, in solution, of the bisulphite compound, from which it is regenerated, in contrast to its isomers verbenone and myrtenal, only by treatment with strong alkali. A further difference lies in the fact that pinocarvone cannot be distilled at ordinary pressure, since under these conditions it undergoes extensive decomposition.

---

* *J. Amer. C.S.* 1941, 63, 3339.

† The "pinocarvone" obtained as the main product of the reaction is, according to Schmidt, actually myrtenal.

For *l*-pinocarvone, from *E. globulus*, Schmidt has given the following constants: m.p. $-1{\cdot}8°$, $d^{15°}$ 0·9875, $n_D^{20°}$ 1·4950, $[\alpha]_D$ $-68°$ (*semicarbazone*, m.p. 350°; *oxime*, m.p. 131–132°). The m.p. of the oxime is not depressed on admixture with nitrosopinene.

d-Pinocarvone, obtained by the oxidation of *β*-pinene with selenium dioxide, has b.p. 84–85°/4 mm., $d_{4°}^{25°}$ 0·981, $n_D^{20°}$ 1·4935, $[\alpha]_D$ $+63°$ (*semicarbazone*, m.p. above 300°; *oxime*, m.p. 132–133°).

Reduction of *l*-pinocarvone with aluminium *iso*propoxide gives *d-cis*-pinocarveol (p. 222).

According to Schmidt, the ketone readily absorbs bromine in chloroform solution to give a *dibromide*, m.p. 74°, $[\alpha]_D$ $+130°$, whilst with simple Grignard reagents it undergoes 1 : 4-addition, to yield homologues of pinocamphone; methyl magnesium bromide, for example, gives (V).*

---

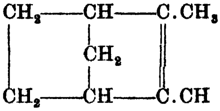
* Treibs, *Ber.* 1944, **77**, 572.

CHAPTER IV

SANTENE AND ITS DERIVATIVES

A. HYDROCARBON

SANTENE



In 1900 Müller[*] made the interesting observation that East Indian sandalwood oil, which is obtained from the wood of *Santalum album* L., contained a hydrocarbon, C_9H_{14}, to which the name santene was given. Later Aschan[†] showed that santene occurred also in Siberian, German and Swedish pine needle oils.

For our knowledge of the constitution of santene we are indebted mainly to the investigations of Semmler and Bartelt.[‡] A consideration of the physical constants of the hydrocarbon led these authors to conclude that it was probably dicyclic and contained one ethylenic linkage. This was proved to be correct by its oxidation with ozone in benzene solution[§] to a *diketone*, $C_9H_{14}O_2$, b.p. 124–127°/9 mm., d^{20° 1·024, $n_D^{20^\circ}$ 1·4665, *disemicarbazone*, m.p. 216°. This diketone must be 1:3-*diacetyl*cyclo*pentane* (II), since on oxidation with an excess of hypobromite it gives trans-cyclo*pentane*-1:3-*dicarboxylic acid* (IV), m.p. 87–88·5°, an acid which was prepared synthetically by Pospischill.[‖] More recently, the diketone itself has been synthesised by Mohunta and Ray.[¶] These reactions show conclusively that santene must be represented by formula (I).

If an excess of sodium hypobromite is not used in the oxidation of the diketone, trans-3-*acetyl*cyclo*pentanecarboxylic acid* (III) (*semicarbazone*, m.p. 168°) is obtained, the structure of which has been confirmed by synthesis.[**] It is of interest to record that when

---

[*] *Arch. Pharm.* 1900, **238**, 366.

[†] *Ber.* 1907, **40**, 4920.

[‡] *Ibid.* 4595; 1908, **41**, 128, 389, 867.

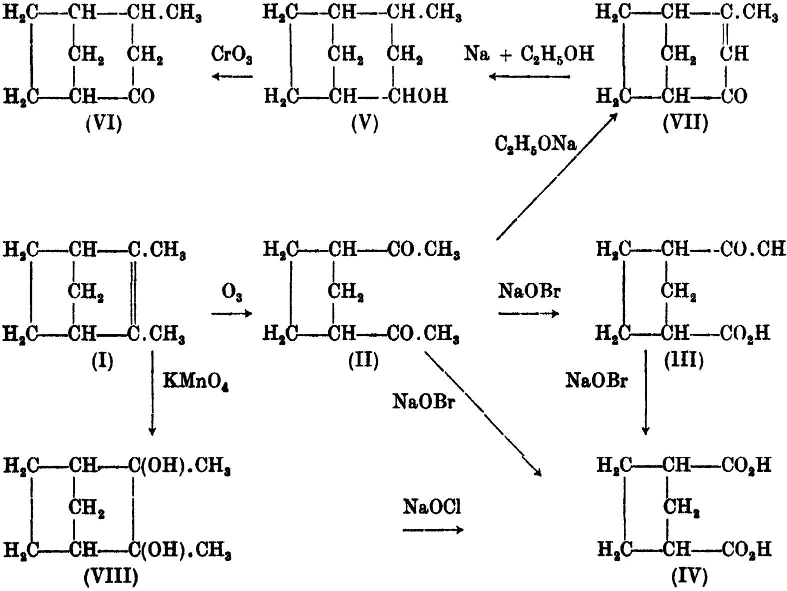
[§] Compare Ruzicka and Liebl, *Helv. Chim. Acta*, 1923, **6**, 271.

[‖] *Ber.* 1898, **31**, 1950.

[¶] *J.C.S.* 1934, p. 1328.

[**] Guha and Ranganathan, *Ber.* 1936, **69**, 1199.

1 : 3-diacetyl*cyclo*pentane is reduced with sodium and alcohol it yields the dicyclic *alcohol*, $C_9H_{16}O$ (V), b.p. 100°/10 mm., $d^{15°}$ 1·1012, $n_D^{15°}$ 1·5004, which gives on oxidation with chromic acid the corresponding *ketone*, $C_9H_{14}O$ (VI), b.p. 91–94°/9 mm., $d^{20°}$ 1·002, n_D 1·4895, *semicarbazone*, m.p. 214°. If, however, the diketone is warmed with sodium ethoxide or with ammonia under pressure an unsaturated *ketone*, $C_9H_{14}O$ (VII), b.p. 104–105°/10 mm., $d^{20°}$ 1·029, $n_D^{20°}$ 1·1513, is formed, the constitution of which is proved by its oxidation with potassium permanganate to cis-3-*acetyl*cyclo*pentane carboxylic acid* (III), and by its reduction with sodium and alcohol to the dicyclic alcohol (V).

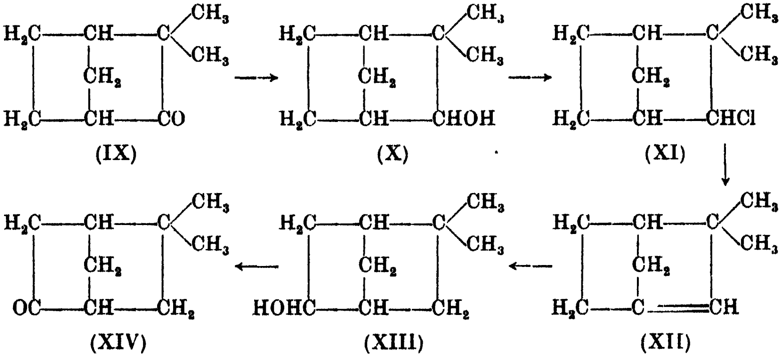


The constitution assigned to santene has been confirmed by its oxidation with potassium permanganate in acetone solution to *santene glycol* (VIII), m.p. 193°, b.p. 135°/10 mm., some 1 : 3-*diacetyl*cyclo*pentane* being also obtained. This alcohol, which has been synthesised by reduction of the diketone (II) with aluminium amalgam,* was found to be remarkably stable to dehydrating agents, but, when boiled with dilute sulphuric acid, it gave a saturated ketone, $C_9H_{14}O$, b.p. 76–80°/10 mm., $d^{20°}$ 0·988, n_D 1·4798, the constitution of which does not appear to have been determined. Palmén[*] has found, however, that when the glycol is heated with concentrated sulphuric acid a small percentage of camphenilone is formed. On oxidation with sodium hypochlorite it gives the dicarboxylic acid (IV).[†] According to Komppa[‡] a stereoisomer of santene glycol, m.p. 194–195°, is formed as a by-product in the preparation of the alcohol (V) by the method referred to above.

---

* Mohunta and Ray, *J.C.S.* 1934, p. 1328.

Santene has been prepared synthetically by methods involving Wagner rearrangements and they are of considerable interest, since they indicate the difficulties which are encountered in investigations in this field. In 1912 Hintikka and Komppa[§] showed that when *camphenilone* (IX) (p. 367) was reduced to the corresponding alcohol, *camphenilol* (X) (p. 369), the chloride, *camphenilyl chloride* (XI), resulting from this on treatment with phosphorus pentachloride,[||] gave on removal of hydrogen chloride a hydrocarbon, to which the name *camphenilene* was given. This was considered by Hintikka and Komppa to have the formula (XII) and by hydration they prepared an alcohol, iso*camphenilol*, which gave on oxidation a ketone, iso*camphenilone*, these being formulated as (XIII) and (XIV) respectively.



---

[*] *Brit. Chem. Abstr.* 1929, A, p. 192.

[†] Palmén, *J. pr. Chem.* 1934 [ii], **141**, 113.

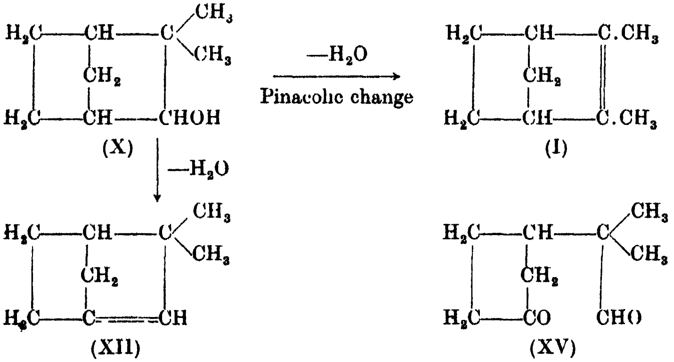
[‡] *Ber.* 1935, **68**, 1127.

[§] *Annalen*, 1912, **387**, 293; compare Jagelki, *Ber.* 1899, **32**, 1503.

[||] The product is more probably apobornyl chloride, which, however, may isomerise into camphenilyl chloride prior to the loss of hydrogen chloride (see p. 370).

It was pointed out by Meerwein[*] that this structure for camphenilene contravened the well-known Bredt rule, and he suggested that in all probability camphenilene was identical with santene. A reinvestigation by Hintikka and Komppa[†] has shown this suggestion of Meerwein to be correct. Camphenilene, which is not quite homogeneous, consists essentially of santene, and its formation from camphenilyl chloride, or more directly by the dehydration of camphenilol, involves a rearrangement. A small amount of *apocyclene* (p. 331) is also present in the reaction products.[‡]

It is not improbable that the santene is contaminated with some camphenilene of structure (XII) since on ozonolysis a ketonic aldehyde is obtained in small quantity, which may be (XV) although its constitution has not been proved. *iso*Camphenilol and *iso*camphenilone are identical with santenol and santenone respectively.



(X) (I) (XII) (XV)

Ruzicka and Liebl[§] have shown that santene can be prepared also from *fenchyl alcohol* (XVI) (p. 552). On dehydration, *fenchyl alcohol* yields two hydrocarbons α- (or D-l-) and β- (or D-d-) *fenchenes*[||] (XVII) and (XVIII), which on ozonolysis yield α- and β-*fenchocamphorones* (XIX) and (XX). By the dehydration of α- and β-*fenchocamphorols* (XXI) and (XXII), which can be

---

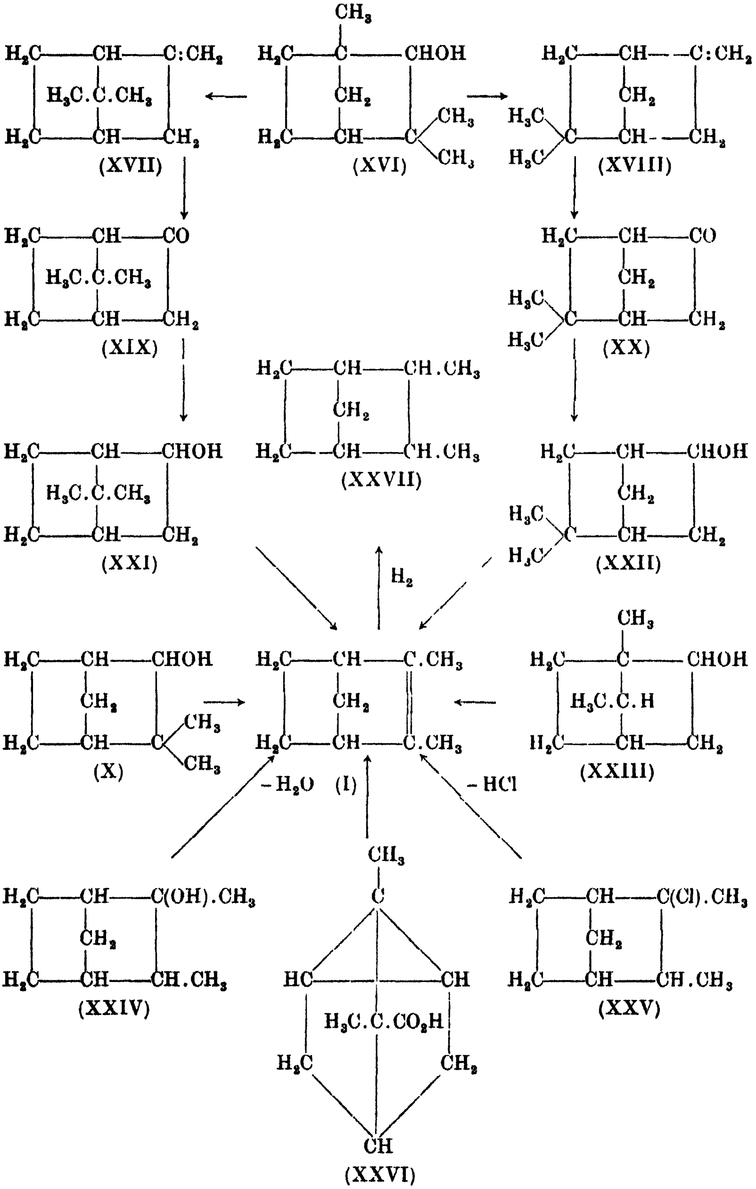
[*] *Annalen*, 1914, **405**, 134.

[†] *Bull. Soc. chim.* 1917 [iv], **21**, 14.

[‡] Gratton and Simonsen, *J.C.S.* 1935, p. 1621; Komppa and Nyman, *Ber.* 1936, **69**, 334; compare Snitter, *Bull. Inst. Pin*, 1933, p. 209; Lipp and Daniels, *Ber.* 1936, **69**, 586. See also Vol. I, p. 4.

[§] *Helv. Chim. Acta*, 1923, **6**, 271.

[||] For the nomenclature of the fenchenes, see p. 534.


(XVII)
(XVI)
(XVIII)
(XIX)
(XX)
(XXVII)
(XXI)
(XXII)
H_2
(X)
(I)
(XXIII)
$-H_2O$
$-HCl$
(XXIV)
(XXV)
(XXVI)

prepared by reduction of the ketones, santene was obtained, the reaction in each case involving a Wagner or Nametkin rearrangement. These reactions are shown in the scheme set out on p. 247 in which, for comparison, *camphenilol* (X) and *santenol* (XXIII) are included.

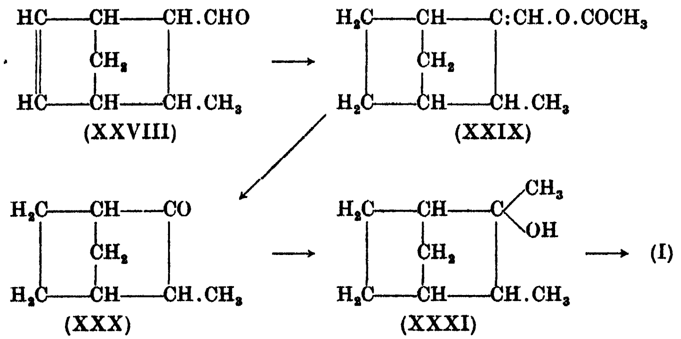
In addition to the methods referred to, santene has also been obtained by the dehydration of *santene hydrate* (XXIV)[*] and by the removal of hydrogen chloride from *santene hydrochloride* (XXV).

Of interest also is its formation, first observed by Müller,[†] by the digestion of *teresantalic acid*, $C_{10}H_{14}O_2$ (XXVI), with sulphuric acid.

Santene can be readily characterised by the preparation of the *nitrosochloride*, m.p. 109–110°,[‡] or the *nitrosite*, m.p. 123–126°.[§]

Santene is an oil possessing a somewhat unpleasant odour. It is difficult to obtain pure and it resinifies somewhat readily. The following constants have been quoted by Aschan and by Semmler: b.p. 140–141°/770 mm., 31–33°/9 mm., $d^{20°}$ 0·863, $n_D^{20°}$ 1·4665. According to Deussen, it can be readily hydrogenated in the presence of a palladium catalyst to yield *santane* (XXVII), b.p. 150–152°, $d^{18·5°}$ 0·8712, $n_D^{18·6°}$ 1·4636.

A direct synthesis of santene has been carried out by Diels and Alder.[‖] Crotonaldehyde was condensed with *cyclo*pentadiene to give the *aldehyde* (XXVIII), which was reduced and converted



---

[*] Aschan, *Öfvers. Finska Vet. Soc.* 1910, **53** (A), no. 8.

[†] *Arch. Pharm.* 1900, **238**, 380; compare Semmler, *Ber.* 1910, **43**, 1898.

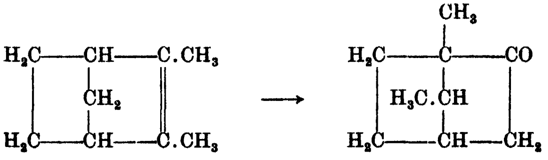
[‡] Aschan, *Ber.* 1907, **40**, 4921.

[§] Deussen, *J. pr. Chem.* 1926 [ii], **114**, 111.

[‖] *Annalen*, 1931, **486**, 205.

into the *enol acetate* (XXIX). Ozonisation of this substance to give 3-*methylnorcamphor* (XXX), followed by condensation with methyl magnesium iodide gave *γ-santenol* (XXXI), a stereoisomer of santene hydrate (p. 256). Dehydration of this alcohol gave santene.

The oxidation of santene with ozone and potassium permanganate has already been referred to. With potassium dichromate-sulphuric acid mixture it gives santenone (XXXII),* a reaction which involves hydration, a Wagner rearrangement, and subsequent oxidation. Deussen has made a preliminary investigation of the products formed by the oxidation of the hydrocarbon with mercuric acetate. The main product of the reaction is the additive compound, $C_9H_{14}OH, HgO_2C.CH_3$, m.p. 126–127°, which when treated with potassium iodide in alcoholic solution yields the corresponding iodide, $C_9H_{14}OH, HgI$, m.p. 130–131°. Other products of the oxidation are santene glycol (VIII) (p. 244) and a substance of the composition $C_9H_{14}O$, which is probably identical with the ketone prepared by Semmler (p. 245) by digestion of santene glycol with dilute sulphuric acid.


(I) (XXXII)

On treatment with bromine, santene yields a *tribromide*, which according to Müller† melts at 62–63°, whilst Aschan‡ found it to melt at 77–80°. This divergence is possibly due to the formation of stereoisomerides, since the bromide is readily crystallised. With hydrogen chloride in ethereal solution santene yields a crystalline *hydrochloride*, which melts at about 80°.§ As mentioned above, the hydrochloride can be reconverted into santene by digestion with aniline, whilst with milk of lime at 70–80° it yields santene hydrate (p. 256).

---

* Aschan, *Öfvers. Finska Vet. Soc.* 1910, **53** (A), no. 8.
† *Arch. Pharm.* 1900, **238**, 370.
‡ *Ber.* 1907, **40**, 4921.
§ Müller, *Arch. Pharm.* 1900, **238**, 371; Aschan, *Ber.* 1907, **40**, 4922.

Santene is not affected by digestion with alkali, but it can be hydrated readily by the Bertram-Walbaum method[*] or by treatment with formic acid,[†] yielding santenol. The hydration can also be effected very conveniently by sulphuric acid in ethereal solution.[‡]

α-Santene nitrosochloride crystallises in blue needles, m.p. 109–110°,[§] which on exposure to the air pass into a colourless β-modification. This is possibly bimolecular since, when heated, it passes over at 90° into the blue α-form.

Santene nitrosite, first prepared by Müller,[‖] crystallises in blue prisms, m.p. 123–126°. Its reactions have been studied by Deussen,[¶] who has found that when it is heated with an alcoholic potassium hydroxide solution it passes into a colourless form, m.p. 105°, which like the blue form is monomolecular. Both forms of the nitrosite yield a *hydrochloride*, m.p. 98°, and can be hydrogenated using a palladium catalyst to give a colourless substance, m.p. 87–88°, having the composition $C_9H_{16}O_3N_2$, the constitution of which has not been determined. Deussen has described also the isolation of a green nitrosite, but its relationship to the blue nitrosite is not known; with alkali it passes into the colourless form, m.p. 105°. According to Onischtschenko[**] the blue nitrosite, on warming in alcoholic solution, gives 1:3-*diacetyl*cyclo*pentane* (p. 243); on long standing in petroleum solution it is converted into a *nitrosate*, m.p. 113–114°.

---

[*] Aschan, *Öfvers. Finska Vet. Soc.* 1910, **53** (A), no. 8.

[†] Semmler and Bartelt, *Ber.* 1908, **41**, 128.

[‡] Deussen, *J. pr. Chem.* 1926 [ii], **114**, 111.

[§] Müller, *Arch. Pharm.* 1900, **238**, 369; Aschan, *Ber.* 1907, **40**, 4921.

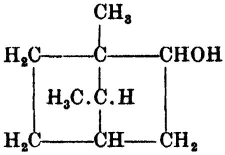
[‖] *Loc. cit.* p. 370.

[¶] *J. pr. Chem.* 1926 [ii], **114**, 111.

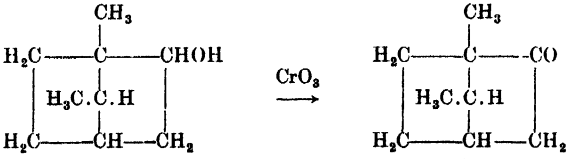
[**] *Bull. Acad. Sci. U.R.S.S.* 1937, p. 209.

B. ALCOHOLS

THE SANTENOLS[*]



In 1910 Schimmel and Co.[†] isolated from East Indian sandalwood oil (from *Santalum album*) an alcohol, $C_9H_{16}O$, m.p. 58–62°, which they called *santenone alcohol.* This alcohol must have the structural formula (I), since on oxidation with chromic acid it yields *santenone* (II), the constitution of which has been definitely established (p. 257).



(I) (II)

Some years previously Semmler and Bartelt[‡] had found that when *teresantalic acid* (IV) was digested with formic acid, a formate was obtained which gave on hydrolysis an alcohol, *π-norborneol*, $C_9H_{16}O$, m.p. 68–70°. This alcohol gave on oxidation santenone (II). They further found that, when santenone was reduced with sodium in ethereal solution, a stereoisomeric alcohol,

---

[*] The nomenclature of the stereoisomeric alcohols, the santenols, having the constitution given at the head of this section, is somewhat confused. For the natural alcohol, m.p. 58–62°, Schimmel and Co. have used the name *santenone alcohol.* Semmler and Bartelt called the two alcohols, m.p. 68–70° and 91–92°, prepared from santene, *π-norborneol* and *π-norisoborneol* respectively, whilst Aschan for an alcohol, m.p. 97–98°, probably identical with Semmler and Bartelt's π-nor*iso*borneol, introduced the name *α-santenol,* calling *santene hydrate* (p. 256) *β-santenol.* This latter designation is unfortunate, since β-santenol is a structural and not a stereoisomeride of α-santenol. Although confusion may arise from the fact that the terms "*norborneol*" and "*norisoborneol*" are applied to the lower homologues, $C_7H_{12}O$, Semmler and Bartelt's nomenclature is retained for the synthetic alcohols, since it has historic priority, whilst the natural alcohol is designated santenone alcohol, as it is doubtful if it is homogeneous. In discussing their common reactions the term santenol will be used.

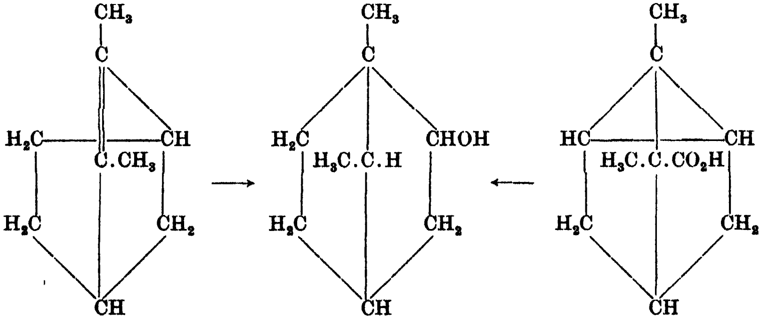
[†] *Schimmel's Report,* 1910, Oct., p. 120.

[‡] *Ber.* 1907, **40,** 4467.

π-*nor*iso*borneol*, m.p. 91–92°, was obtained, which also gave santenone on oxidation. It was suggested by Semmler and Bartelt that these two alcohols were related to one another in the same manner as borneol and *iso*borneol (p. 353). In the same year, Aschan[*] prepared π-nor*iso*borneol, m.p. 97–98°, by the hydration of santene (III) by the Bertram-Walbaum method. This latter reaction involves a Wagner rearrangement,[†] whilst in the preparation from teresantalic acid (IV) decarboxylation, accompanied by fission of a *cyclo*propane ring, occurs. The alcohol prepared by Aschan's method was probably a mixture, since, prior to crystallisation, it melted at 80–81°.

A mixture of π-norborneol and π-nor*iso*borneol can be obtained also by the hydration of santene with formic acid[‡] or with a mixture of ether and sulphuric acid.

The santenols have an odour resembling that of borneol and camphor and can be identified by oxidation to santenone, which is readily characterised (see p. 258).



(III) (I) (IV)

The optically active santenols do not appear to have been described, the activity which has been observed in specimens prepared from santene being due to the presence of impurities.

From the melting-points of the alcohol which have been given already, it will have been observed that these show considerable variations. This is probably due in part to the difficulties encountered in its purification, but also to the occurrence of stereoisomerides, four *dl*-forms of which are possible. Komppa[*] has purified the santenol obtained by the hydration of santene by the Bertram-Walbaum method, through the crystalline *santenyl hydrogen diphenate*, m.p. 119–120°. The alcohol obtained by the hydrolysis of this derivative melts sharply at 86°. Whilst there appears to be no doubt as to the purity and homogeneity of this santenol, its preparation does not show that π-norborneol, m.p. 68–70°, and π-nor*iso*borneol, m.p. 97–98°, do not exist. Although not necessarily pure, they are probably stereoisomeric with Komppa's alcohol, and support is lent to this view by the fact that, whereas Aschan's alcohol, m.p. 97–98°, gave a *phenylurethane*, m.p. 61–62°, that prepared by Schimmel and Co. from an alcohol melting at approximately the same temperature, 84–86°, as that of Komppa, gave a *phenylurethane*, m.p. 83°. It must be pointed out, however, that by the reduction of β-santenone (p. 259) with sodium and alcohol, Komppa and Nyman[†] have obtained a so-called *β-santenone alcohol*, m.p. 95°, b.p. 192–195° (*phenylurethane*, m.p. 91–92°), whilst Enkvist[‡] has described yet another stereoisomer, m.p. 105–106°, obtained by the isomerisation of α-santenol with sodium ethoxide. It is evident that some of these alcohols must be mixtures of stereoisomers, and further work is obviously required to elucidate their relationship to one another and also the natural alcohol. According to Komppa and Beckmann,[§] the degree of association in solution, as measured by molecular weight determination, may provide useful evidence in this field, since it is partly dependent upon the configuration of the solute.

---

[*] *Ber.* 1907, **40**, 4923.

[†] Compare Ruzicka and Liebl, *Helv. Chim. Acta*, **1923**, **6**, 271.

[‡] Semmler and Bartelt, *Ber.* 1908, **41**, 128.

In view of the recent progress which has been made in the investigation of the stereochemistry of the santenic acids (see below), a careful study of the oxidation of the various santenols would be of considerable interest. Aschan's santenol was readily oxidised with potassium permanganate in alkaline solution[‖] to give cis-*santenic acid* (V), m.p. 170–171°, which yields an *anhydride*, m.p. 115–116°.

---

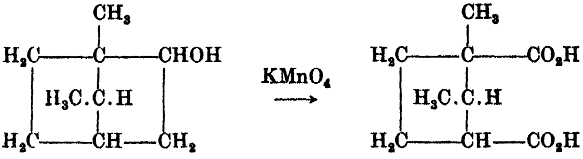
[*] *Ber.* 1929, **62**, 1751.

[†] *Chem. Zentr.* 1937, II, 3759.

[‡] *J. pr. Chem.* 1933 [ii], **137**, 261.

[§] *Annalen*, 1936, **522**, 137.

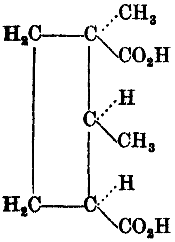
[‖] Aschan, *Öfvers. Finska Vet. Soc.* 1910–1911, **53** (A), no. 8, p. 18; Komppa and Hintikka, *Bull. Soc. Chim.* 1917 [iv], **21**, 17.



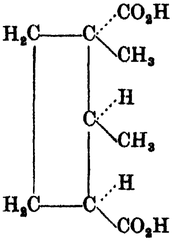
(I) (V)

This acid was accompanied by an isomer, termed iso*santenic acid*, m.p. 121–123°, which was thought to be the *trans*-modification, but according to Enkvist[*] it is a mixture of santenic and *allo*santenic acids.

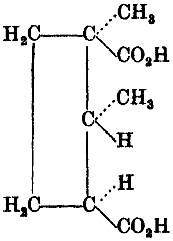
The santenic acids can exist in four *dl*-modifications, and as a result of several more recent investigations in this field[†] the following configurations have been allocated to them, on the basis that *cis-allo*santenic acid forms an anhydride more readily than *cis*-santenic acid:



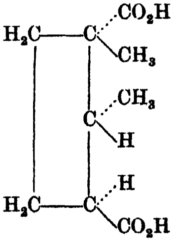
cis-Santenic acid
m.p. 170–171°
(Anhydride,
m.p. 115–116°)



trans-Santenic acid
m.p. 166–167°



*cis-allo*Santenic acid
m.p. 151–152°
(Anhydride,
m.p. 93–94°)



*trans-allo*Santenic acid
m.p. 129–130°

The *cis*-acids may be transformed into the corresponding *trans*-isomers by heating with hydrochloric acid in acetic acid solution.[‡]

The structure of santenic acid has been confirmed[§] by a synthesis based on the classical method used by Komppa in the camphoric acid series (p. 382). The condensation product (VI) of oxalic ester and dimethyl β-methylglutarate on treatment with methyl iodide and sodium methoxide gave (VII), which on reduction first with sodium amalgam, and then with phosphorus and hydriodic acid, was converted into the *dehydrosantenic acid* (VIII), m.p. 197–198°. On hydrogenation over platinum this gave mainly *cis-allo*santenic acid (V), m.p. 151–152°.

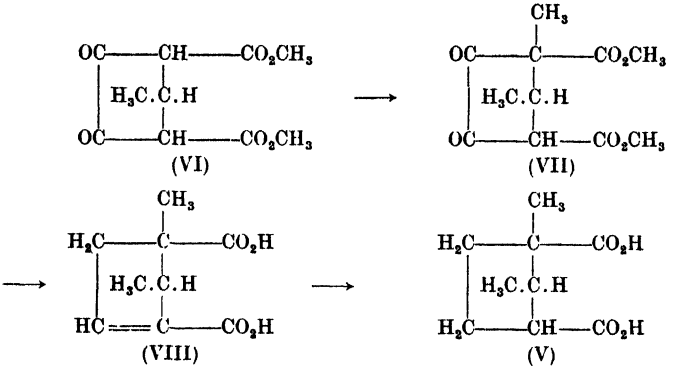
---

[*] *Finska Kem. Medd.* 1932, **41**, 74.

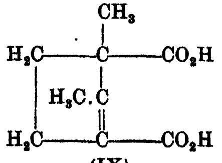
[†] Enkvist, *J. pr. Chem.* 1933 [ii], **137**, 261; Komppa, *Ber.* 1932, **65**, 1708; 1934, **67**, 828; Komppa and Rohrmann, *Annal. Acad. Sci. Fennicae*, 1935, A **44**, nos. 3 and 10.

[‡] Compare, however, Ishidate and Sano, *Ber.* 1941, **74**, 1189.

[§] Enkvist, *J. pr. Chem.* 1933 [ii], **137**, 261; Komppa and Rohrmann, *Ber.* 1934, **67**, 828; *Brit. Chem. Abstr.* 1938, A II, 22. For an alternative method of synthesis, see Chakravarti, *J. Ind. C.S.* 1943, **20**, 243.


(VI) (VII) (VIII) (V)

On bromination, santenic acid gives a monobromo-derivative, which loses hydrogen bromide on treatment with quinoline to give a dehydrosantenic acid (the "*santenenic acid*" of Aschan), m.p. 169–170°, which is a structural isomeride of (VIII). On hydrogenation it gives a mixture of santenic acids, the main product being the *cis-allo*-isomer; since this differs from the original santenic acid in the configuration at the carbon atom in the position β- to the carboxyls, the dehydro-acid, m.p. 169–170°, must contain an ethylenic linkage which involves this position, and it is therefore formulated as (IX).


(IX)

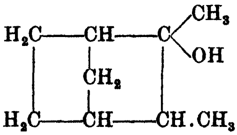
With phosphorus pentachloride in light petroleum solution, π-norborneol was found by Semmler and Bartelt[*] to give a *chloride*, m.p. 59–61°, b.p. 72–73°/10 mm., from which, by the action of alkali, santene could be obtained. This reaction involves a Wagner rearrangement in the reverse direction to that occurring in the formation of norborneol from santene.

---

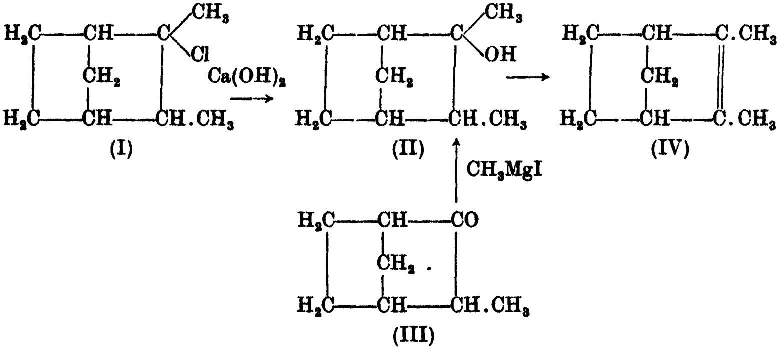
[*] *Ber.* 1908, 41, 128.

A number of esters of santenol have been described, but these are undoubtedly mixtures of stereoisomerides, so that it is unnecessary to refer to their properties in detail. They resemble in odour the corresponding derivatives of borneol.

SANTENE HYDRATE



Santene hydrate, $C_9H_{16}O$, for which Aschan[*] has suggested the name β-santenol, does not occur in nature. It was prepared by Aschan[†] by the action of milk of lime at 70–80° on *santene hydrochloride* (I) (p. 249). A stereoisomeric alcohol, γ-santenol, m.p. 63–65°, has been prepared by Diels and Alder[‡] by the action of methyl magnesium iodide on 3-methylnorcamphor (III) (see p. 249).



The constitution of santene hydrate (II) (and of its stereoisomerides) is established by its method of preparation and by the fact that on dehydration with either acetic acid or oxalic acid it yields *santene* (IV). Santene hydrate crystallises from alcohol in needles, m.p. 101–102°, b.p. 192°, and has an odour reminiscent of nonyl alcohol. The alcohol prepared by Aschan showed slight optical activity, but this was probably due to a trace of impurity, since the santene employed for its preparation was itself slightly active.

---

[*] *Medd. K. Vetenskapsakad. Nobel-Inst.* 1919, 5, no. 8, p. 27.

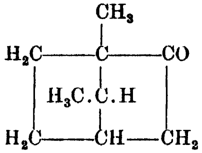
[†] *Öfvers. Finska Vet. Soc.* 1910, 53(A), no. 8, p. 9.

[‡] *Annalen*, 1931, 486, 205.

Santene hydrate is very resistant to oxidising agents and is not attacked by potassium permanganate. With chromic acid partial dehydration to santene occurs, but the products formed are mainly resinous.

C. *KETONE*

SANTENONE (*π-NORCAMPHOR*)*



l-Santenone, $C_9H_{14}O$, has been shown by Schimmel and Co.[†] to occur in East Indian sandalwood oil. An optically inactive form of this ketone had been prepared some years previously by Semmler and Bartelt,[‡] who called it *π-norcamphor*, by the oxidation with chromic acid of the alcohol, *π-norborneol* (p. 251). Subsequently Aschan[§] found that it could be obtained more conveniently by the oxidation of santene with potassium dichromate-sulphuric acid mixture. These reactions have already been formulated on pp. 247, 249 and need not be repeated here.

The constitution of santenone (I) has been established by its oxidation with potassium permanganate to *santenic acid* (II), whilst the presence in it of a methylene group adjacent to the carbonyl group has been confirmed by the preparation of *hydroxymethylene* and *benzylidene* derivatives (see p. 258).

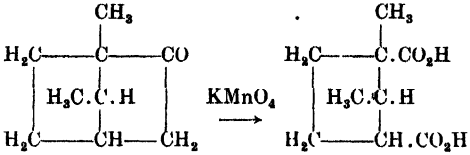
---

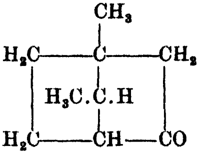
[*] It should be noted that the term "*norcamphor*" is applied to the parent ketone, $C_7H_{10}O$.

[†] *Schimmel's Report*, 1910, Oct., p. 98.

[‡] *Ber.* 1907, **40**, 4467.

[§] *Öfvers. Finska Vet. Soc.* 1910, **53** (A), no. 8, p. 17.

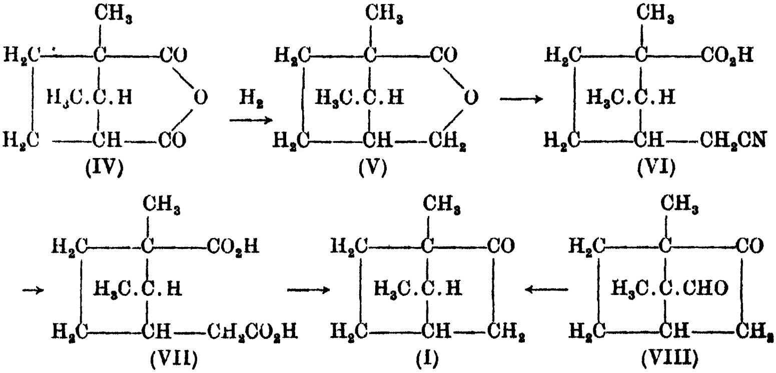

(I) (II)


(III)

It must be pointed out that these results would be equally readily explained if santenone were represented by formula (III), which bears the same relationship to epicamphor as santenone does to camphor. The assignment, however, of this formula to the ketone would make it extremely difficult to account for its formation by the oxidation of santene and for the hydration of the hydrocarbon to santenol.

A synthesis of santenone, based on the classical method used in the camphor series (p. 382) has been described by Enkvist.[*] *Santolide* (V), m.p. 41–42°, was prepared by the hydrogenation of santenic anhydride (IV), and converted by treatment with potassium cyanide into *homosantenonitrile* (VI), m.p. 103°, hydrolysed to *homosantenic acid* (VII), m.p. 165°.[†] Santenone, m.p. 50° (*semicarbazone*, m.p. 228–229°), was then obtained by heating the calcium salt of the acid.

l-Santenone from natural sources has m.p. 58–61°, b.p. 193–195°, $[\alpha]_D$ −4·4° (in alcohol), and gives a *semicarbazone*, m.p. 222–224°. By the autoxidation of *π-ketocamphor* (VIII), Ishidate

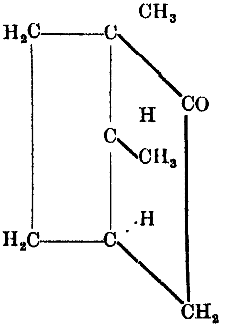

(IV) (V) (VI) (VII) (I) (VIII)

---

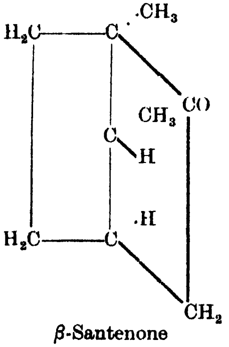
[*] *J. pr. Chem.* 1933 [ii], 137, 261.

[†] For an alternative synthesis of homosantenic acid, see Sen-Gupta, *J. Indian C.S.* 1933, 10, 341.

and Sano[*] have obtained a d-*santenone*, m.p. 56–59°, $[\alpha]_D^{22^\circ}$ + 11·4° (in alcohol), *semicarbazone*, m.p. 235–236°. It may be that this is not the enantiomorph of the natural ketone, but a stereoisomer, since two forms of santenone are likely to exist. Evidence of such isomerism has indeed been known for some time, since the inactive form, according to Aschan,[†] has m.p. 50–52°, b.p. 197°, whereas Semmler and Bartelt[‡] found m.p. about 30°, b.p. 75–76°/9 mm., d^{20° 0·966, $n_D^{20^\circ}$ 1·4690, for a specimen prepared by the oxidation of π-norborneol. It is only recently, however, that efforts have been made to obtain the isomerides in a pure state, and it has been shown[§] that crude *dl*-santenone semicarbazone may be separated by fractional crystallisation into two forms, which on hydrolysis give α-*santenone*, m.p. 55–56° (*semicarbazone*, m.p. 235–236°; *oxime*, m.p. 74°) and β-*santenone*, m.p. 49–50° (*semicarbazone*, m.p. 236–237°; *oxime*, m.p. 50–51°). On oxidation, these give respectively santenic and *allo*santenic acids, and on the basis of the configurations given for these acids on p. 254, the following stereochemical relationships may be allocated to the ketones:



α-Santenone



β-Santenone

In view of the close structural relationship to camphor the reactions of santenone are of great interest, but the difficulties involved in its preparation have so far precluded the carrying out of any extensive investigations. Most of the reactions now to be described, however, will be found to resemble closely those in the camphor series.

---

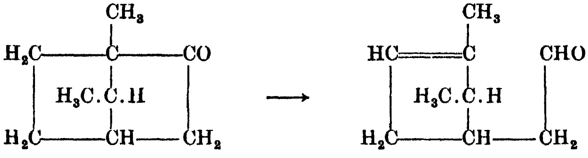
[*] *Ber.* 1941, **74**, 1189.

[†] *Öfvers. Finska Vet. Soc.* 1910, **53** (A), no. 8, p. 16.

[‡] *Ber.* 1907; **40**, 4466.

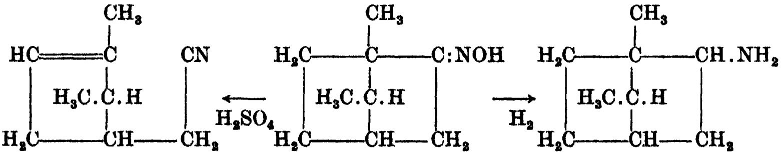
[§] Aschan, *Svensk. Kem. Tidskr.* 1933, **45**, 209; Komppa and Nyman, *Chem. Zentr.* 1937, II, 3759.

The reduction of santenone with sodium and alcohol yields one or more of the stereoisomerides of santenol (see p. 251), whilst, as already mentioned, its oxidation with potassium permanganate gives santenic acid. According to Rimini,[*] it is oxidised on exposure to sunlight with the formation of an unsaturated aldehyde (IX) but the constitution of this has not been rigidly proved. The reaction with selenium dioxide is referred to on p. 262.



(I) (IX)

l-*Santenoneoxime* is an oil, b.p. 110–113°/6 mm.,[†] but Rimini[‡] has obtained the inactive oxime as a crystalline solid, m.p. 80–81°; this was previously described by Semmler and Bartelt[§] as an oil, b.p. 116–120°/9 mm., $d^{20°}$ 1·012, $n_D^{20°}$ 1·4956, and it is rather remarkable that the melting-point quoted by Rimini should be higher than that of either of the individual isomers to which reference has been made above. By the reduction of the liquid oxime (X) with sodium and alcohol, Semmler and Bartelt prepared *santenylamine* (*π-norbornylamine*) (XI), b.p. 69°/10 mm., $d^{20°}$ 0·9163, $n_D^{20°}$ 1·4761, *picrate*, m.p. 208°, whilst by the action of sulphuric acid they obtained the *nitrile* (XII) of π-norcampholenic acid, b.p. 82–83°/9 mm., $d^{20°}$ 0·950, n_D 1·4720. This nitrile gave on hydrolysis with alkali *π-norcampholenic acid*, b.p. 132–134°/10 mm., $d^{20°}$ 1·014, n_D 1·4793.



(XII) (X) (XI)

---

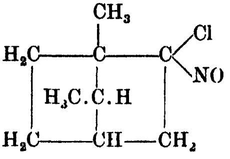
[*] *Gazzetta*, 1914, **44**, I, 568.

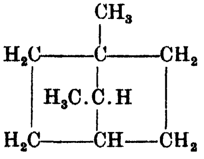
[†] Schimmel and Co. *loc. cit.*

[‡] *Gazzetta*, 1913, **43**, II, 522.

[§] *Ber.* 1908, **41**, 127.

The action of nitrous acid in hydrochloric acid solution on the crystalline oxime was investigated by Rimini, who obtained in place of the expected pernitrososantenone, a blue oil, b.p. 113–116°/9 mm., having the composition $C_9H_{14}ONCl$. This oil on treatment with semicarbazide gives santenone semicarbazone, and it is possibly represented by formula (XIII).


(XIII)


(XIV)

Komppa and Hasselström[*] have described a liquid *santenone hydrazone* (*acetyl* derivative, m.p. 152–153°) which on reduction with sodium ethoxide gave the hydrocarbon, *santenane* (XIV), m.p. 66–67°, b.p. 146–148°.

Pernitrososantenone was prepared by the method adopted for the preparation of the corresponding derivative of thujone.[†] It is an oil which cannot be purified, and gives on hydrolysis with alkali a mixture of santenoneoxime and santenone. Acid hydrolysis gave, in addition to santenone, an isomeric ketone, *isosantenone*, b.p. 185–186°, *semicarbazone*, m.p. 172–175°. The constitution of this ketone was not determined.

iso*Nitrososantenone* (XV), m.p. 89–90°, has been prepared by Palmén[‡] and yields on degradation by the usual methods derivatives of santenic acid.[§] Hydrolysis with hydrochloric acid in the presence of formaldehyde gave *santenonequinone* (XVI), m.p. 84–85°, which forms a *hydrate*, m.p. 137–138°, *disemicarbazone*, m.p. 238°, *dioxime*, m.p. 144–145°.[‖] A diketone having presumably the same structure was prepared by Semmler and Bartelt[¶] by the oxidation of *benzylidenesantenone* (XVII) with potassium permanganate in acetone solution. According to these authors it melts at 105°, b.p. 121–127°/10 mm. This difference in properties is probably due to stereoisomerism, a supposition which could readily be verified by oxidation to the stereoisomeric santenic acids.

---

[*] *Annalen*, 1932, **496**, 164.

[†] *Gazzetta*, 1900, **30**, I, 602.

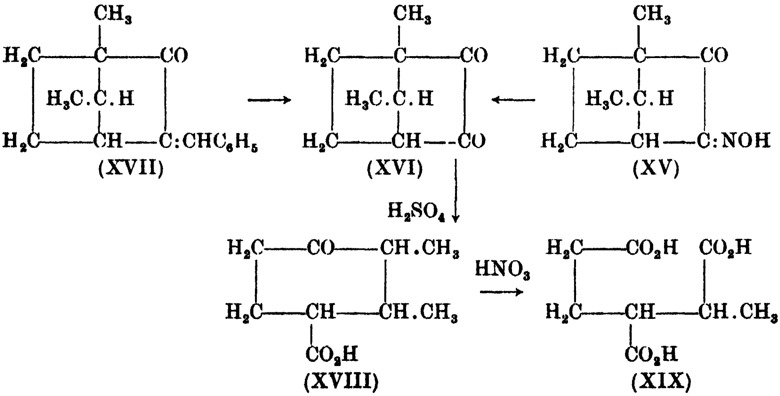
[‡] *Dissertation*, Helsingfors, 1914.

[§] Compare Aschan, *Naphtenverbindungen, Terpene und Campherarten*, 1929, p. 142.

[‖] Palmén, *Finsk. Kem. Medd.* 1927, **36**, 11.

[¶] *Ber.* 1908, **41**, 125.

The quinone, m.p. 84–85°, obtained by Palmén, may be prepared more conveniently by the oxidation of santenone with selenium dioxide.[*] It readily forms a *quinoxaline* derivative, m.p. 102–103°, with *o*-phenylenediamine, and on treatment with sulphuric acid undergoes rearrangement to the *keto-acid* (XVIII), m.p. 132° (*semicarbazone*, m.p. 192°), which on oxidation with nitric acid gives pentane-$\beta\gamma\epsilon$-tricarboxylic acid (XIX). The structures of both acids have been confirmed synthetically by Chakravarti. This rearrangement is of particular interest in view of similar studies which have been carried out on camphorquinone (p. 469).


(XVII) (XVI) (XV)

(XVIII) (XIX)

A d-*santenonequinone*, m.p. 73–74°, b.p. 110–112°/12 mm., $[\alpha]_D^{16^\circ}$ $-75{\cdot}4^\circ$ (in alcohol), has been obtained by the oxidation of *d*-santenone with selenium dioxide;[†] on oxidation with hydrogen peroxide it gives d-cis-*santenic acid*, m.p. 151–152°, $[\alpha]_D^{33^\circ}$ $+38{\cdot}3^\circ$ (in alcohol) (*anhydride*, m.p. 129–130°).

Semmler and Bartelt[‡] prepared *hydroxymethylenesantenone*, b.p. 110–113°/9 mm., by the action of *iso*amyl formate on the ketone in the presence of sodium.

Enkvist[§] has shown that the sodio-derivative of santenone, on treatment with carbon dioxide, gives *santenone carboxylic acid*

---

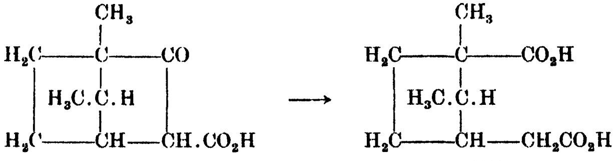
[*] Chakravarti, *J. Ind. C.S.* 1944, **21**, 319.

[†] Ishidate and Sano, *Ber.* 1941, **74**, 1189.

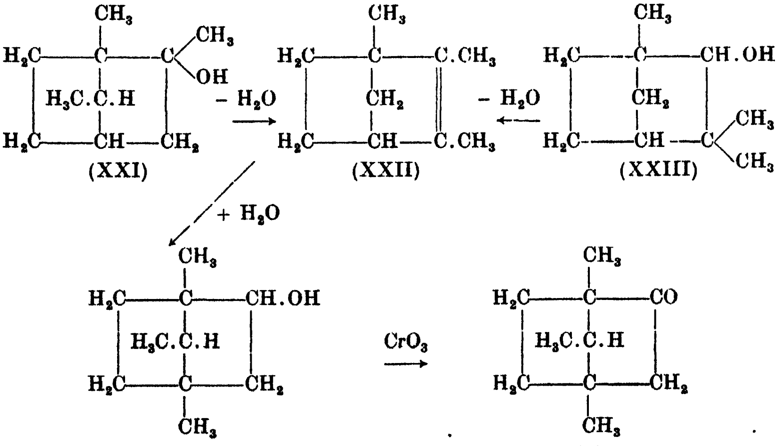
[‡] *Ibid.* 1907, **40**, 4468.

[§] *J. pr. Chem.* 1933 [ii], **137**, 261.

(XX), m.p. 109°, the diethyl ester of which undergoes ring fission on treatment with sodium ethoxide to give *homosantenic acid* (VII). By the use of cyanogen in place of carbon dioxide, the corresponding nitrile may be obtained.


(XX) (VII)

Komppa and Nyman* have studied in some detail the reactions of tert-1-*methylsantenyl alcohol* (XXI), m.p. 77–79°, b.p. 82–83°/10 mm., and of the numerous products which may be derived from it. Reference can be made here to only a few of these compounds, and for further information the original literature may be consulted. The tertiary alcohol is obtained from santenone by the action of methyl magnesium iodide; on dehydration it gives 1-*methylsantene* (XXII), b.p. 151–152°, which has also been obtained and studied by Toivonen,† who observed its formation on dehydration of *fenchyl alcohol* (XXIII) over aluminium phosphate or kaolin. Hydration of 1-methylsantene gives sec.-4-



(XXI) (XXII) (XXIII)

(XXIV) (XXV)

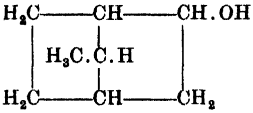
---

* *Annalen*, **1935, 517,** 105; **518,** 204; *Ber.* **1936, 69,** 712; **1939, 72,** 16.

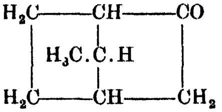
† *Suomen. Kem.* **1935, 88,** 44; **1936, 9 B,** 15.

methylsantenol (XXIV), oxidised by chromic acid to 4-methylsantenone (XXV). This alcohol and ketone can exist in stereoisomeric forms, and some progress has been made in their characterisation.

Mention may also be made here of the lower homologues, *aposantenol* (XXVI) and *aposantenone* (XXVII), which have been synthesised and their stereoisomerism and reactions investigated by Komppa and Beckmann.[*]



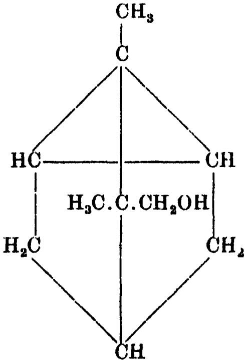
(XXVI)

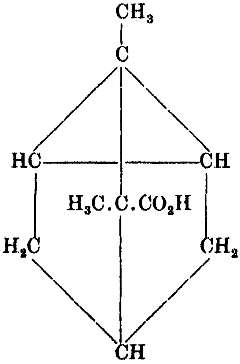


(XXVIII)

D. RELATED TRICYCLIC COMPOUNDS

TERESANTALOL AND TERESANTALIC ACID





Teresantalic acid, $C_{10}H_{14}O_2$, was isolated from sandalwood oil (obtained from *Santalum album*) practically simultaneously by Soden and Müller[†] and by Guerbet.[‡] *Teresantalol*, $C_{10}H_{16}O$, was subsequently shown to be present in this oil,[§] although it had previously been prepared by Semmler and Bartelt[||] by reduction of methyl teresantalate with sodium and alcohol.

---

[*] *Annalen*, 1936, **523**, 68.

[†] *Arch. Pharm.* 1900, **238**, 303.

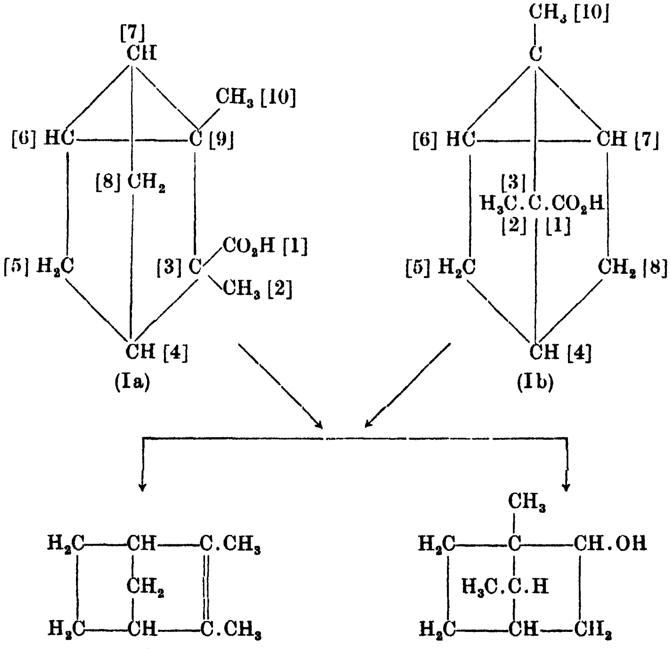
[‡] *Compt. rend.* 1900, **130**, 417.

[§] *Schimmel's Report*, 1910, Oct., p. 106; 1911, April, p. 105.

[||] *Ber.* 1907, **40**, 3102, 4465.

Teresantalic acid, m.p. 157°, b.p. 183°/28 mm., $[\alpha]_D^{18^\circ}$ -77° (in benzene), is very resistant to the action of oxidising agents, but on digestion with hot dilute sulphuric acid it is converted into *santene* (II), whilst with formic acid the formate of *santenol* (III) is obtained, together with a lactone, m.p. 191°, the structure of which is discussed on p. 267.

These observations led Semmler and Bartelt to propose that teresantalic acid might be represented by either the "camphene" formula (Ia) or the "camphor" formula (Ib).


(Ia) (Ib)

(II) (III)

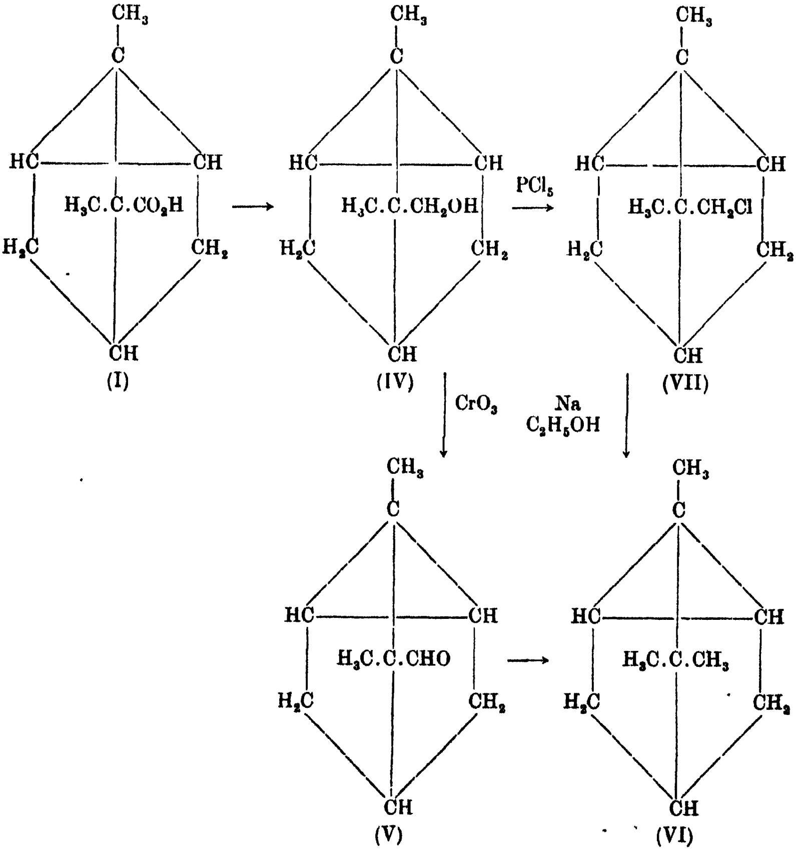
It was pointed out by Ruzicka and Stoll* that these two formulae merely represent two different projections of the same three-dimensional model and are therefore identical; this is made clear by the numbering of the carbon atoms in the two formulae (Ia) and (Ib).

---

* *Helv. Chim. Acta*, **1922, 5, 928.**

This constitution for teresantalic acid has been confirmed by Ruzicka and Liebl.* *Teresantalol* (IV), m.p. 114°, b.p. 95–98°/9 mm., $[\alpha]_D$ + 12° (in alcohol) was prepared by reduction of methyl teresantalate, and oxidised with chromic acid to teresantalal (V), the *semicarbazone* (m.p. 217°) of which was then treated with sodium ethoxide at 180° to yield a hydrocarbon which was identified as *tricyclene* (VI). The liquid hydrocarbon obtained by Semmler, by reduction of *teresantalyl chloride* (VII) with sodium and alcohol, was probably an impure form of tricyclene.

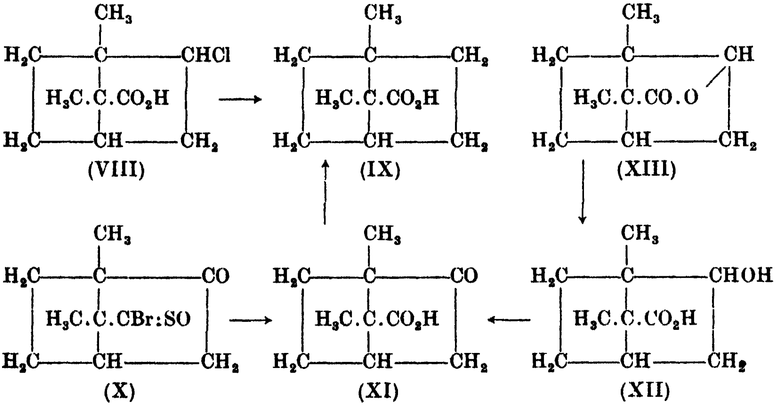
Teresantalic acid is readily attacked by hydrogen chloride in methyl alcoholic solution, fission of the *cyclo*propane ring



---

* *Helv. Chim. Acta*, **1926**, **9**, 140.

occurring with the formation of a *hydrochloroteresantalic* acid, m.p. 199°, which is probably one of the possible stereoisomerides of formula (VIII) since on reduction with sodium and alcohol it gives *dihydroteresantalic acid* (IX), m.p. 229°. The structure of the latter acid has been confirmed by a synthesis described by Hasselström;[*] π-bromocamphorsulphoxide (X), m.p. 137°, was oxidised with potassium permanganate to iso*ketopinic acid* (XI), m.p. 250°, the semicarbazone of which on treatment with sodium ethoxide gave dihydroteresantalic acid (IX), m.p. 227°. Reference has already been made to the observation of Semmler and Bartelt that treatment of teresantalic acid with formic acid gives, in addition to santenol, a crystalline *lactone*, m.p. 191°.[†] This substance, which, according to Hasselström,[‡] is preferably obtained from methyl teresantalate under the same conditions, on treatment with alkali, followed by acidification, gives the corresponding *hydroxy-acid*, m.p. 195–196°, to which formula (XII) must be assigned, since Hasselström has shown that on oxidation it gives a stereoisomer, m.p. 270°, of *iso*ketopinic acid (XI),[§] reduced through the semicarbazone to dihydroteresantalic acid.


(VIII) (IX) (XIII)

(X) (XI) (XII)

---

[*] *Ann. Acad. Sci. Fennicae,* 1929, A **30**, no. 12; compare Wedekind and Stüsser, *Ber.* 1923, **56**, 1557.

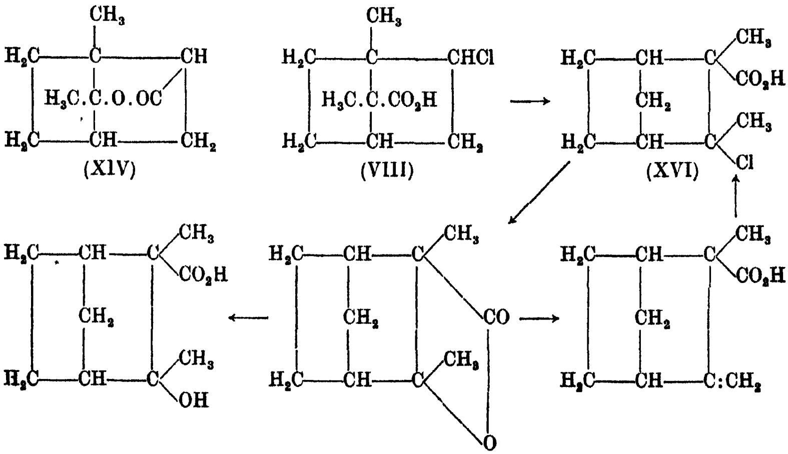
[†] See also Lipp, *Chem. Ber.* 1947, **80**, 165.

[‡] *J. Amer. C.S.* 1931, **53**, 1097.

[§] Some authors prefer to retain the term *iso*ketopinic acid for the *trans*-isomer, m.p. 250° (in which the carboxyl group and the π-methyl group in formula (XI) would be interchanged), and use the systematic name, cis-π-*apocamphor*-7-*carboxylic acid* for the *cis*-isomer, m.p. 270°. For simplicity, *cis*-formulae are used throughout the present account for this acid and related compounds, irrespective of the actual configuration of the substance under discussion.

Both stereoisomers of the keto-acid (XI) have also been encountered by Asahina and Ishidate,[*] who have made the interesting observation that the *semicarbazone*, m.p. 255°, of their *iso*ketopinic acid, m.p. 250°, $[\alpha]_D$ $+3°$ (in alcohol) on reduction with sodium ethoxide gives laevorotatory dihydroteresantalic acid, m.p. 231°, $[\alpha]_D^{27°}$ $-18°$ (in alcohol), whilst the *semicarbazone*, m.p. 215–216°, of the stereoisomeric keto-acid, m.p. 272°, $[\alpha]_D^{24°}$ $+67°$ (in alcohol) gives the enantiomorphous dihydroteresantalic acid, m.p. 231°, $[\alpha]_D^{25°}$ $+18°$ (in alcohol).

The constitution (XIII) now assigned to the lactone, m.p. 191°, differs from that (XIV) originally proposed by Semmler and Bartelt who were of the opinion that formula (XIII) represented an isomeric lactone, m.p. 103°, obtained by Müller by the action of cold alkali on hydrochloroteresantalic acid (VIII). This so-called "Müller lactone" has recently been reinvestigated by Asahina, Ishidate and Momose,[†] who conclude that it is a β-lactone (XV) in the form of a mixture of stereoisomerides derived from the rearranged hydrochloride (XVI). This hydrochloride was not isolated, but has been prepared indirectly (see below) and shown to give the Müller lactone when dissolved in cold alkali. On treatment of the lactone with hot alkali it passes into a mixture of the corresponding *β-hydroxy-acid* (XVII), m.p. 185°,



(XIV) (VIII) (XVI)

(XVII) (XV) (XVIII)

---

[*] *Ber.* 1933, 66, 1673.

[†] *Ibid.* 1935, 68, 559.

$[\alpha]_D^{19^\circ}$ −5·8° (in alcohol) and *apocamphenecarboxylic acid* (XVIII), m.p. 142°, $[\alpha]_D^{18^\circ}$ −68·8° (in benzene). Furthermore,* the latter acid is stereoisomeric with a product, m.p. 142°, $[\alpha]_D$ −127·6° (in benzene), which had been obtained by Rupe and Tomi† by the action of aniline on methyl hydrochloroteresantalate, and termed by them iso*teresantalic acid*; this acid‡ was originally thought to be a stereoisomer of teresantalic acid.

Apocamphenecarboxylic acid on oxidation with chromic acid gives santenone, and hydration with a mixture of sulphuric and acetic acids gives the γ-hydroxy-acid (XII) as a mixture of stereoisomers. One of these, termed l-cis-*π-apoborneol*-7-*carboxylic acid* is obtained in the form of the lactone (XIII), m.p. 191°, readily separated from the trans-*isomer*, m.p. 288°, $[\alpha]_D^{18^\circ}$ −47·3° (*acetate*, m.p. 122°); on oxidation, these give the corresponding stereoisomeric forms of *iso*ketopinic acid (XI), m.p. 270° and 250° respectively. A third stereoisomer of the γ-hydroxy-acid (XII) is obtained by the reduction with sodium and alcohol of *iso*ketopinic acid, m.p. 250°; it has m.p. 273°, $[\alpha]_D^{18^\circ}$ +4° (in alcohol), is a *trans*-acid, differing from the acid, m.p. 288°, in the configuration of the hydroxyl group, and its bromide on treatment with aniline gives the same apocamphenecarboxylic acid $[\alpha]_D$ −71° as that obtained from the Müller lactone. When apocamphenecarboxylic acid is treated in methyl alcoholic solution with hydrogen chloride it gives the hydrochloride (XVI), m.p. 174°, $[\alpha]_D^{18^\circ}$ −84·3° (in alcohol), in quantitative yield.

The term "*iso*teresantalic acid" is still retained for the stereoisomer of apocamphenecarboxylic acid, and its properties have been further investigated by Steiger and Rupe.§ For a rigorously purified sample they give m.p. 137°, $[\alpha]_D^{20^\circ}$ −150·8° and for the *methyl ester*, b.p. 91°/10 mm., $[\alpha]_D^{2^\circ}$ −133·5° (homogeneous) (*mercuri-acetate compound*, m.p. 214°). It is worthy of note that the melting-point of *iso*teresantalic acid is not depressed by admixture with apocamphenecarboxylic acid. On hydrogenation under various conditions, *iso*teresantalic acid gives rise to two different *dihydroisoteresantalic acids*, m.p. 106–107° and 121–122°, neither of which is identical with dihydroteresantalic acid.[*]

---

* Asahina, Ishidate and Momose, *Ber.* 1935, **68**, 83; compare Asahina and Ishidate, *ibid.* p. 555; Asahina, Ishidate and Sano, *ibid.* 1936, **69**, 343.

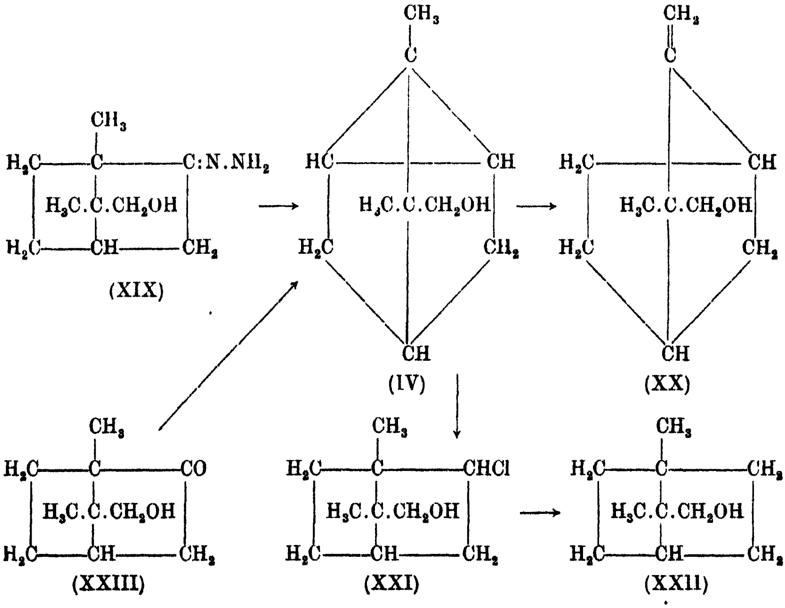
† *Ber.* 1916, **49**, 2563.

‡ It is of interest to note that this isomer, together with some teresantalic acid, is formed by the dehydration of the β-hydroxy-acid (XVII).

§ *Helv. Chim. Acta*, 1937, **20**, 1117.

Teresantalic acid is a degradation product of α- and β-santalene and of α-santalol (Vol. III); it has also been obtained[†] by the oxidation of the hydrazone of *iso*ketopinic acid with mercuric oxide.

d-*Teresantalol*, obtained by reduction of methyl teresantalate, has m.p. 114°, b.p. 95–98°/9 mm., $[\alpha]_D$ +12° (in alcohol). dl-*Teresantalol*, m.p. 118°, has been prepared[‡] by the oxidation of trans-π-*hydroxycamphor hydrazone* (XIX) with mercuric oxide. When heated with dilute sulphuric acid, teresantalol gives *apocamphenecarbinol* (XX), m.p. 146°, whilst with hydrogen chloride it gives a product, m.p. 125–126° (without purification), which is probably mainly 2-*chlorocamphan*-8-ol (XXI); on re-



---

[*] *Helv. Chim. Acta*, 1937, **20**, 1117.

[†] Asahina, Ishidate and Momose, *Ber.* 1935, **68**, 83.

[‡] Asahina and Ishidate, *Ber.* 1935, **68**, 947; Guha and Bhattacharyya, *J. Ind. C.S.* 1944, **21**, 271.

duction with sodium and alcohol this gives *dihydroteresantalol* (XXII), m.p. 171°,[*] which may also be prepared by the reduction of dihydroteresantalic acid (IX) with the same reagents.[†]

Both d- and l-*dihydroteresantalols*, m.p. 200·5°, $[\alpha]_D$ ± 17° (in alcohol), have been prepared[‡] by reduction of the semicarbazones of *cis*- and *trans*-π-hydroxycamphors (XXIII) (see p. 431).

dl-*Dihydroteresantalal*, m.p. 172–173° (*semicarbazone*, m.p. 214–215°), is obtained by the oxidation of dihydroteresantalol with chromic acid.

[*] Hasselström, *J. Amer. C.S.* 1931, **53**, 1097.

[†] Semmler and Bartelt, *loc. cit.*

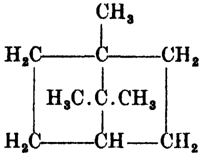
[‡] Asahina and Ishidate, *Ber.* 1934, **67**, 71.

CHAPTER V

CAMPHANE, *ISO*CAMPHANE AND THEIR DERIVATIVES

A. HYDROCARBONS

CAMPHANE



The saturated dicyclic hydrocarbon, camphane, $C_{10}H_{16}$, is of outstanding importance, since it is the parent hydrocarbon of the camphor group. Attempts to prepare this hydrocarbon by the direct reduction of camphor have not proved successful, but it has been obtained by methods which leave no doubt that it must contain the same ring structure as the ketone.

The impure hydrocarbon (II) was first prepared by Letts[*] and almost simultaneously by Montgolfier[†] by the action of sodium on molten bornyl chloride (I), being later obtained pure by Kachler and Spitzer[‡] by reduction of the chloride in benzene solution with sodium. Semmler[§] later showed that camphane was formed when either bornyl chloride, *iso*bornyl chloride or bornyl dichloride was reduced with sodium in alcoholic solution, whilst Aschan[||] has described its preparation by the reduction of bornyl iodide with zinc dust in acetic-hydriodic acid solution. This latter method of preparation has the advantage that it is performed at the ordinary temperature and so minimises the risk of molecular rearrangement. Reduction of bornyl chloride has also been observed to occur when the chloride is allowed to react with magnesium and the product subsequently treated with cyanogen.*

---

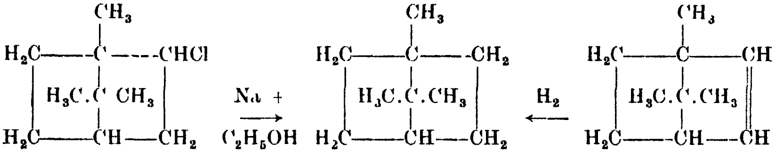
[*] *Rep. Brit. Assoc.* 1876; *Ber.* 1880, **13**, 793.

[†] *Ann. Chim.* 1880 [v], **19**, 145.

[‡] *Ber.* 1880, **13**, 615, 2236.

[§] *Ibid.* 1900, **33**, 777, 3424; compare Meerwein and Wortmann, *Annalen*, 1924, **435**, 205.

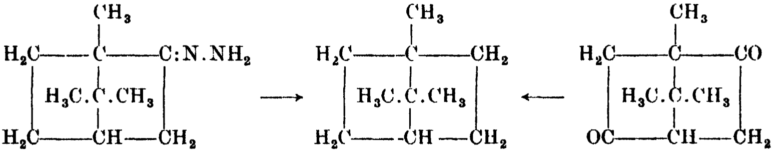
[||] *Ber.* 1900, **33**, 1009; 1912, **45**, 2395; *Annalen*, 1901, **316**, 234.



(I) (II) (III)

Henderson and Pollock† have shown that camphane can be conveniently prepared by the hydrogenation of *bornylene* (III) by the Sabatier-Senderens process, using a nickel catalyst and a temperature of 170–190°.

A direct proof of the structural relationship of camphane to camphor has been furnished by Kishner‡ and by Wolff,§ who prepared the hydrocarbon from *camphorhydrazone* (IV), the decomposition of the hydrazone being effected either by distillation with potassium hydroxide or by the action of sodium ethoxide at 190°. A somewhat similar method is involved in its preparation from the *dihydrazone* of the *diketone* (V) (see p. 393).‖



(IV) (II) (V)

Camphane crystallises in six-sided plates, m.p. 156–156·5°, b.p. 160–161°/760 mm., and it is extremely volatile even at the ordinary temperature. It has a faint odour resembling that of borneol. The hydrocarbon is optically inactive whatever its method of preparation, and this is in agreement with theory, since its molecule contains a plane of symmetry. It is extremely resistant to most reagents and it is not attacked by fuming sulphuric acid at 180°. Nitro-derivatives have, however, been prepared by the action of dilute nitric acid at 145–150°. This reaction, which was first studied by Konowalov and Kikina,[*] was investigated further by Nametkin,[†] who showed that two stereoisomeric nitrocamphanes (VI) and (VII) are formed. *α-Nitrocamphane* melts at 128–130° and *α′-nitrocamphane* at 146–147°; they are separable by fractional crystallisation and both on oxidation yield *dl*-camphor.

---

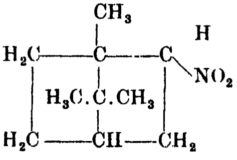
* Grignard, Bellet and Courtot, *Ann. Chim.* 1919 [ix], **12**, 374.

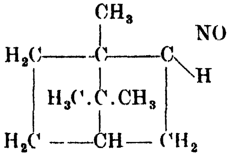
† *J.C.S.* 1910, **97**, 1620.

‡ *J. Russ. Phys. Chem. Soc.* 1911, **43**, 582.

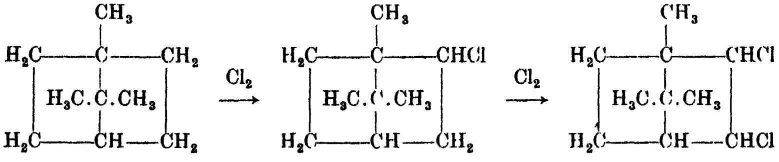
§ *Annalen*, 1912, **394**, 95.

‖ Bredt and Goeb, *J. pr. Chem.* 1920 [ii], **101**, 278.

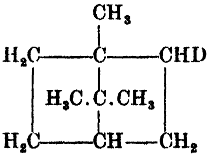

(VI)

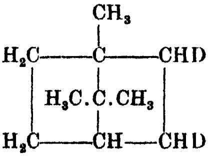

(VII)

Gandini[‡] has shown that camphane reacts with chlorine in carbon tetrachloride solution to give *bornyl chloride* (I); further action results in the formation of 2:3-*dichlorocamphane* (VIII), m.p. 126°.


(II) (I) (VIII)

2-*Deuterocamphane* (IX), m.p. 156°, has been prepared[§] by the treatment of *l*-bornyl magnesium chloride with deuterium oxide, whilst 2:3-*dideuterocamphane* (X) is obtained by the reduction of *l*-bornylene (III) with deuterium.[‖] Neither product shows any appreciable optical activity, which supports the view that the


(IX)


(X)

---

[*] *J. Russ. Phys. Chem. Soc.* 1902, **34**, 935.

[†] *Ibid.* 1915, **47**, 409.

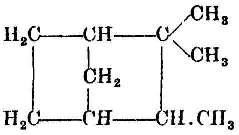
[‡] *Gazzetta*, 1936, **66**, 357.

[§] Biilmann, Jensen and Knuth, *Ber.* 1936, **69**, 1034; Biilmann, Jensen and Bak, *ibid.* p. 1947.

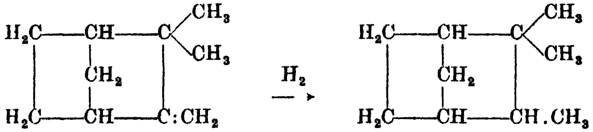
[‖] Leffler and Adams, *J. Amer. C.S.* 1936, **58**, 1555.

replacement by deuterium of one or more hydrogen atoms in a non-resolvable compound, to give a structure which no longer possesses any of the essential elements of symmetry, does not result in stereochemical asymmetry.

ISO*CAMPHANE* (*DIHYDROCAMPHENE*)



Owing to the marked tendency of camphene and its derivatives to isomerise to substances containing the camphane nucleus, considerable difficulty was experienced in the preparation of the saturated hydrocarbon, *iso*camphane or dihydrocamphene (II), $C_{10}H_{18}$. The early experiments made with the object of preparing this hydrocarbon had as their starting-point substances, such as bornyl chloride, containing the camphane nucleus, and impure *iso*camphane was probably first obtained by Semmler[*] by heating borneol with zinc dust under pressure. The introduction of catalytic methods of hydrogenation has rendered it possible to prepare this hydrocarbon by less drastic reactions.


(I) (II)

In 1901, Sabatier and Senderens[†] hydrogenated *camphene* (I), m.p. 41°, with a nickel catalyst at 160–175°, and obtained a saturated hydrocarbon, b.p. 164–165°, $d_{4^\circ}^{0^\circ}$ 0·849, which probably consisted essentially of *iso*camphane. This method of reduction was also used by Zelinski[‡] who, from a *d*-camphene, m.p. 49–50°, obtained a crystalline hydrocarbon, m.p. 60–61°, which was slightly dextrorotatory and consisted undoubtedly of pure *iso*-

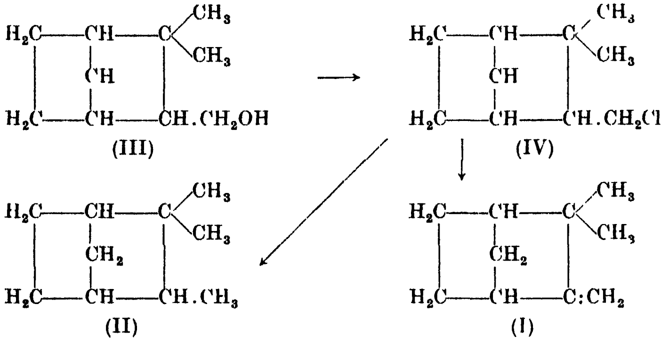
---

[*] *Ber.* 1900, **33**, 776.

[†] *Compt. rend.* 1901, **132**, 1256; *Ann. Chim.* 1905 [viii], **4**, 391.

[‡] *J. Russ. Phys. Chem. Soc.* 1904, **36**, 768; Zelinski and Gutt, *Ber.* 1907, **40**, 4747.

camphane. Shortly afterwards Semmler[*] prepared a mixture of camphene and *iso*camphane by a somewhat different method. He converted *camphenilylcarbinol* (III) into the corresponding *chloride* (IV), which on reduction gave a mixture of the two hydrocarbons (I) and (II).



In 1911, Lipp[†] studied in detail the preparation and properties of *iso*camphane and showed the apparently divergent results of Sabatier and Senderens and of Zelinski to be due to the use by the former of an impure camphene.[‡] He found that when carefully purified camphene was reduced over a nickel catalyst at 170–190°, or at the ordinary temperature in the presence of platinum black, a crystalline *iso*camphane was obtained, accompanied by only a small quantity of a liquid hydrocarbon, which was probably *cyclo*fenchene (p. 550). By the reduction of optically active camphene an optically active *iso*camphane was obtained, which was opposite in sign to the unsaturated hydrocarbon. *iso*Camphane has been prepared by Ipatiev[§] by the reduction of camphene at high pressures at 240°, using a nickel oxide catalyst, and also from *d*-borneol with a mixed alumina-nickel oxide catalyst at 110 atmospheres with a temperature of 215–220°. In the latter case *l*-*iso*camphane was obtained. According to Meerwein and Emster[‖] tricyclene on distillation over nickel at 180–200° in a current of hydrogen yields *iso*camphane.

dl-*iso*Camphane melts at 65–66°, b.p. 164·5°/709 mm., $d_{4^\circ}^{67^\circ}$ 0·8275, $n_D^{67^\circ}$ 1·4418, whilst for the optically active modifications the following constants have been observed: *d-iso*camphane, m.p. 62–63°, b.p. 166–166·5°/760 mm., $[\alpha]_D$ +8·68°; *l-iso*camphane, m.p. 63–64·5°, b.p. 164°/757 mm., $d^{20°}$ 0·8417, $[\alpha]_D$ −8·5° (in alcohol).[*]

---

[*] *Ber.* 1909, **42**, 962.

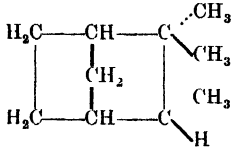
[†] *Annalen*, 1911, **382**, 265.

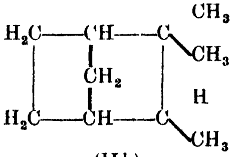
[‡] Compare Henderson and Pollock, *J.C.S.* 1910, **97**, 1622.

[§] *Ber.* 1912, **45**, 3206.

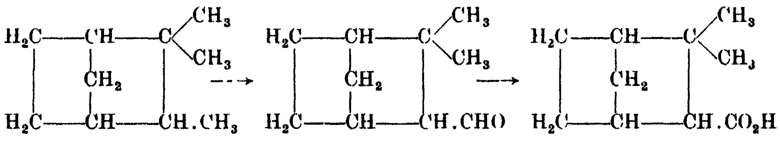
[‖] *Ibid.* 1920, **53**, 1820.

Although only one form of *iso*camphane has apparently been obtained, it is theoretically capable of existing in both the *endo*- (IIa) and *exo*- (IIb) configurations. According to Alder and Stein[†] the known form is the *endo*-modification.


(IIa)


(IIb)

Although the preparation of the optically active modifications of *iso*camphane provided evidence that it contained an asymmetric structure and so differed from camphane, the constitution assigned to it was confirmed by Lipp from a study of its degradation products. On oxidation with potassium permanganate in acetic acid solution it was found to yield a mixture of *camphenilanaldehyde* (V), *camphenilanic* and iso*camphenilanic acids* (VI), whilst by the action of nitric acid it gave the same products as camphene (p. 311), *camphene nitrosite, carboxyapocamphoric acid* and iso*camphoronic acid.* The mechanism of this reaction is discussed on p. 312.


(II) (V) (VI)

When *iso*camphane is heated with magnesium chloride solution under pressure at 400° partial dehydrogenation is observed.[‡]

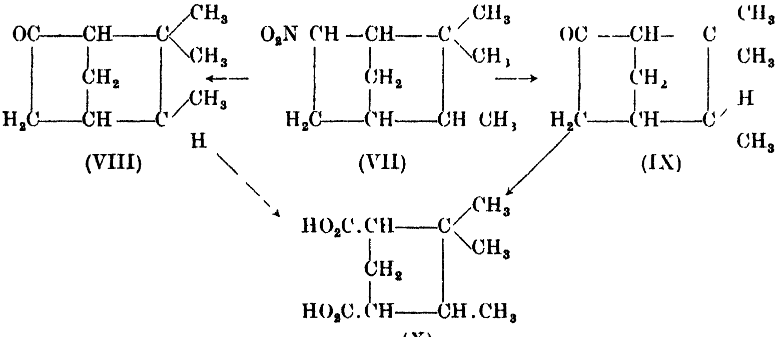
---

[*] The high melting-point, 87°, recorded by Vavon (*Compt. rend.* 1909, **149**, 998) for *iso*camphane prepared by the hydrogenation of camphene with a platinum black catalyst was probably due to his having used an impure specimen of camphene, his hydrocarbon consisting essentially of camphane.

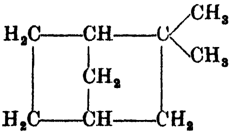
[†] *Annalen*, 1936, **525**, 203.

[‡] Ipatiev and Pines, *J. Amer. C.S.* 1945, **67**, 1931.

The nitration of *iso*camphane has been investigated by Nametkin and Abakumovskaja,[*] who obtained a *nitro*iso*camphane*, m.p. 48–49°. This substance probably has formula (VII), since on oxidation with potassium permanganate it yields a mixture of two stereoisomeric ketones, β-iso*camphone* (VIII), m.p. 91–92°, *semicarbazone*, m.p. 196–197°, and β′-iso*camphone* (IX), m.p. 63–64°, *semicarbazone*, m.p. 195°. The structural identity of the two ketones, which are also formed during the nitration of the hydrocarbon, was established by their oxidation to the same dibasic acid, 1 : 2 : 2-*trimethyl*cyclo*pentane*-3 : 5-*dicarboxylic acid* (X), m.p. 178–180°.


(VIII) (VII) (IX) (X)

CAMPHENILANE



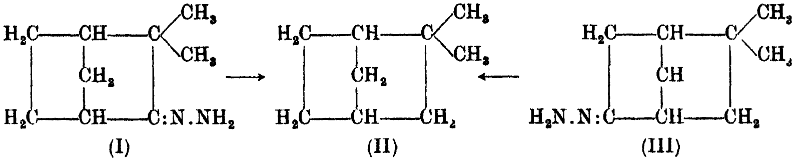
The saturated dicyclic hydrocarbon, camphenilane, C_9H_{16} (II), was prepared by Nametkin[†] by Kishner's method from *camphenilone hydrazone* (I), its constitution following from its method of preparation. It has also been obtained in a similar manner from β-fenchocamphorone hydrazone (III).[‡]

---

[*] *J. Russ. Phys. Chem. Soc.* 1915, **47**, 414.

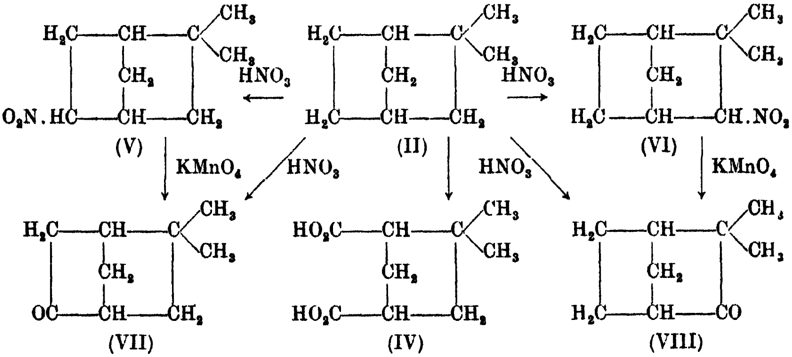
[†] *Annalen*, 1924, **438**, 186; compare Nametkin and Chuchrikova, *J. Russ. Phys. Chem. Soc.* 1915, **47**, 425; Nametkin and Alexandrov, *Annalen*, 1928, **467**, 191.

[‡] Komppa and Hasselström, *Annalen*, 1932, **496**, 164.



Camphenilane is an oil, m.p. 17·5°, b.p. 142·5°/753 mm., $d_{4°}^{20°}$ 0·8547, $n_D^{20°}$ 1·4555, $[\alpha]_D^{20°}$ $-11·2°$ (in alcohol), $-12·3°$ (in benzene). It is extremely stable to nitric acid and resembles in this respect the paraffins. When treated with this reagent ($d = 1·015$) at 140–145° it gives a mixture of two nitrocamphenilanes, two isomeric ketones, $C_9H_{14}O$, and a dibasic acid.

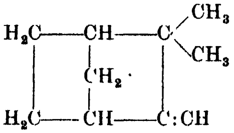
The acid was identified as cis-*apofenchocamphoric acid* (IV), m.p. 144·5–145°. The two nitrocamphenilanes, *α-nitrocamphenilane* (V), m.p. 18–20°, b.p. 124·5–125°/20 mm., and *2-nitrocamphenilane* (VI), m.p. 89–91°, were orientated by oxidation to the corresponding ketones. α-Nitrocamphenilane was found to yield *β-fenchocamphorone* (VII), m.p. 60–63°, identical with the ketone prepared by Komppa and Roschier* from apocyclene (p. 332), whilst 2-nitrocamphenilane gave *camphenilone* (VIII). These two ketones were also formed directly by the action of nitric acid on camphenilane.



---

* *Annalen*, 1922, **429**, 175.

CAMPHENE



Camphene, $C_{10}H_{16}$, is the only crystalline dicyclic hydrocarbon occurring in nature and, for this reason, it is the only terpene hydrocarbon which is easily obtained pure and free from isomerides. *l*-Camphene was first separated by Gobolov[*] from the essential oil derived from *Abies Sibirica*, and the *d*-, *l*- and *dl*-forms have since been shown to occur fairly widely distributed.[†] Camphene had been prepared in the laboratory many years prior to its discovery in nature. It was mentioned on p. 106 that when dry hydrogen chloride is allowed to react with oil of turpentine, a crystalline hydrochloride, "artificial camphor", $C_{10}H_{16}$, HCl, is obtained. After the preparation of this substance by Kindt[‡] in 1802, experiments were instituted with the object of removing the halogen, and in 1831 Oppermann,[§] by the action of lime and other bases, obtained a partially crystalline hydrocarbon of the composition $C_{10}H_{16}$, which undoubtedly contained camphene. These experiments were repeated by Dumas[||] who introduced the name *camphene* or *camphogene* for the hydrocarbon so obtained. It is unnecessary to do more than refer to the later researches of Blanchet and Sell,[¶] Dumas and Oppermann,[**] Souberain and Capitaine,[††] and we may pass on to a consideration of the classical work of Berthelot. In 1858[‡‡] Berthelot first prepared pure camphene by heating "artificial camphor" with an excess of sodium stearate or sodium benzoate in sealed tubes at 240–260°. He described it as a crystalline solid, m.p. 46°, b.p. 160°, which, when oxidised in the presence of platinum black, gave camphor. He made the further important observation that, whereas "artificial camphor" from terebenthine (*l*-pinene) gave *l*-terecamphene (*l*-camphene), that prepared from australene (*d*-pinene) gave *d*-austracamphene (*d*-camphene). It is remarkable evidence of the genius of Berthelot that he recognised at this early date that pinene and camphene could not have the same structural formulae and that "artificial camphor" did not contain the original structure of pinene. The full implication of this interpretation of his results was not appreciated for many years, "artificial camphor" being still referred to as a derivative of pinene. The elimination of hydrogen chloride from "artificial camphor" was investigated by Riban,[*] who succeeded for the first time in preparing *dl*-camphene from *dl*-pinene, and he studied in some detail the reactions of both the optically active and inactive forms of the hydrocarbon. It is not improbable that he was the first to prepare the true camphene hydrochloride, since he remarked on the facility with which the product prepared by the action of hydrogen chloride on camphene decomposed. In the years following, the conditions governing the removal of hydrogen chloride from "artificial camphor" (bornyl chloride) were studied by numerous investigators,[†] and in view of its technical importance the reaction has formed the subject of many patents.

---

[*] *J. Russ. Phys. Chem. Soc.* 1888, **20**, 585.

[†] Gildemeister and Hoffmann, *Die Ätherischen Öle*, I, 317.

[‡] *Trommsdorf J. Pharm.* 1803, **11**, II, 132.

[§] *Pogg. Annalen*, 1831, **22**, 193.

[||] *Annalen*, 1833, **6**, 245.

[¶] *Ibid.* p. 259.

[**] *Ibid.* 1834, **9**, 59.

[††] *Ibid.* 1840, **34**, 311.

[‡‡] *Compt. rend.* 1858, **47**, 266.

Although Berthelot had shown in 1858 that camphene gave on oxidation camphor, and it was well known that the latter could be reduced to borneol, attempts to convert the alcohol into camphene by direct elimination of water are not recorded in the earlier literature. It is true that Riban[‡] prepared "borneocamphene" from the hydrochloride resulting from the action of hydrogen chloride on borneol, but its identity with the camphene derived from "artificial camphor" would appear to have been first recognised by Wallach[§] and by Brühl.[||] Oppenheim and Pfaff[¶] investigated the action of phosphorus pentoxide on borneol and described a hydrocarbon, "borneene", which was probably impure camphene, since Wallach showed definitely[*] that camphene was formed in this reaction.

---

[*] *Ann. Chim.* 1875 [v], **6**, 353.

[†] *Inter al.*, Wallach, *Annalen*, 1887, **239**, 6; Bouchardat and Lafont, *Bull. Soc. chim.* 1887 [ii], **47**, 489; Bruhl, *Ber.* 1892, **25**, 147; Marsh and Stockdale, *J.C.S.* 1890, **57**, 964; Marsh and Gardner, *ibid.* 1891, **59**, 648, 730; Reychler, *Bull. Soc. chim.* 1896 [iii], **15**, 371.

[‡] *Ann. Chim.* 1875 [v], **6**, 353.

[§] *Annalen*, 1885, **230**, 233; 1887, **239**, 6; 1888, **245**, 209; 1889, **252**, 140; 1892, **269**, 349.

[||] *Ber.* 1892, **25**, 148.

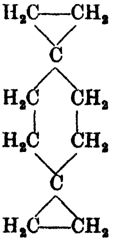
[¶] *Ibid.* 1874, **7**, 626.

The elimination of hydrogen chloride from bornyl and *iso*bornyl chlorides provides the most important method for the preparation of camphene, but it is obtained also in other reactions to which reference will be made in the sequel.

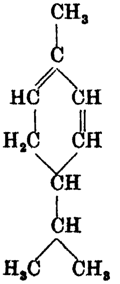
Although camphene can be prepared readily in a crystalline form, doubts were raised from time to time as to whether the hydrocarbon was actually homogeneous and if the hydrocarbons prepared by different reactions were structurally identical. The exhaustive investigations of Aschan[†] leave no doubt that this is the case; *d*-, *l*- and *dl*-camphenes, whatever their origins, have the same constitution.

Since camphene shows such a marked tendency to undergo intramolecular rearrangement, the determination of its constitution has afforded considerable difficulty and has given rise to a large volume of controversial literature, much of which it will be unnecessary to consider here.

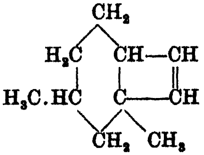
In view of Berthelot's observation that camphene gave on oxidation camphor, it is natural that all the earlier constitutional formulae for the hydrocarbon were based on that of the ketone. The remarkable stability of the camphor structure, as compared with that of pinene and the other hydrocarbons known at the time, led Hlasiwetz[‡] to represent camphene as a saturated hydrocarbon (I) and other tricyclic formulae were suggested at a much later date. In 1873 Kekule[§] suggested (II) containing two ethylenic linkages, the formula being based upon the facile con-



(I)



(II)



(III)

---

[*] *Annalen*, 1885, **230**, 237.

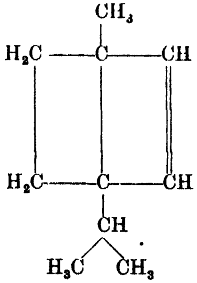
[†] *Ibid.* 1911, **383**, 39.

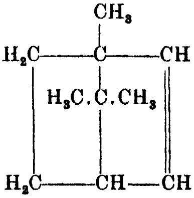
[‡] *Ber.* 1870, **3**, 539.

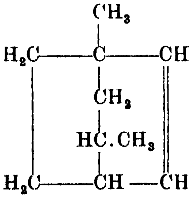
[§] *Ibid.* 1873, **6**, 931.

version of camphor into derivatives of benzene, whilst we owe to Armstrong[*] the suggestion of a dicyclic structure with one ethylenic linkage (III).

The investigations of Kannonikov[†] on the molecular refraction of camphor, borneol and their derivatives had shown them to contain a saturated structure, and it followed therefore that the elimination of water from borneol must yield either a tricyclic saturated hydrocarbon or a dicyclic hydrocarbon containing one ethylenic linkage. Brühl[‡] was at first inclined to the former alternative, but four years later[§] he agreed with the conclusion, at which Wallach[||] had previously arrived, that camphene was a dicyclic hydrocarbon containing one ethylenic linkage. In conformity with the structure at the time assigned to camphor, formula (IV) was suggested for the hydrocarbon, but in 1893 Bredt[¶] with the advent of his new camphor formula modified this to (V).


(IV)


(V)


(VI)

This formula received general acceptance, although tricyclic formulae were suggested by Collie,[**] Marsh and Gardner,[††] and Dodge.[‡‡] Prior to the investigations of Wagner, which must now be discussed, the only important alternative formula advanced was (VI), due to Bouveault.[§§]

In 1890, Wagner[||||] showed that camphene, on oxidation with dilute potassium permanganate, gave a glycol, *camphene glycol*,

---

[*] *Ber.* 1878, **11**, 1698.

[†] *J. Russ. Phys. Chem. Soc.* 1883, **15**, 469; *J. pr. Chem.* 1885 [ii], **32**, 511.

[‡] *Ber.* 1888, **21**, 177.

[§] *Ibid.* 1892, **25**, 168.

[||] *Annalen*, 1887, **239**, 51; 1889, **252**, 136; 1892, **269**, 345.

[¶] *Ber.* 1893, **26**, 3047.

[**] *Ibid.* 1892, **25**, 1108.

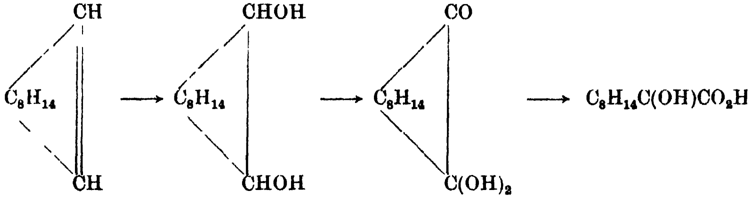
[††] *J.C.S.* 1896, **69**, 74.

[‡‡] *Amer. Chem. J.* 1902, **24**, 649.

[§§] *Bull. Soc. chim.* 1893 [iii], **7**, 403; 1894 [iii], **11**, 134.

[||||] *Ber.* 1890, **23**, 2311.

$C_{10}H_{16}(OH)_2$, thus for the first time furnishing direct experimental evidence of the presence of an ethylenic linkage in the hydrocarbon, and some years later* he described the acids formed during the oxidation. He separated (i) a dibasic acid, *camphenic acid* (camphene-camphoric acid), $C_{10}H_{16}O_4$, isomeric with camphoric acid, and (ii) a hydroxy acid, *camphenylic acid*, $C_{10}H_{16}O_3$, which was an α-hydroxy acid, since it gave, on further oxidation with lead peroxide, a ketone, *camphenilone*, $C_9H_{16}O$. On the basis of the Bredt formula (V) it was somewhat difficult to account for the formation of this hydroxy acid, although a possible mechanism involving the scheme set out below was suggested:



This explanation was obviously unsatisfactory, and it was also extremely difficult to account for the isomerism of camphoric and camphenic acids. In 1899, Wagner† made the revolutionary suggestion that camphor and camphene had not the same carbon skeleton and that, just as there was an intramolecular change in the passage of α-pinene (VII) to bornyl chloride and borneol (VIII) (compare p. 156) so also an intramolecular change occurred in the dehydration of the latter to camphene, which he now represented by (IX). On the basis of this new formula its oxidation to campheneglycol (X), camphenylic acid (XI) and camphenilone (XII) was to be anticipated, but the formation of camphenic acid, to which formula (XIII) was given, was evidently abnormal.

This new formula for camphene, which only differed from that (XIV) suggested by Tiemann‡ in the position of the ethylenic linkage, received considerable support from the further investigations of Wagner and Brickner.§ The elimination of hydrogen chloride from bornyl chloride by the action of alkali does not take place very readily and involves heating the reactants. The sole product of the reaction is, however, camphene. Wagner and Brickner found, however, that, if bornyl iodide (XV) was used instead of the chloride, the reaction proceeded with much greater facility and resulted in the formation, not only of camphene, but also of a new isomeric hydrocarbon, *bornylene*,[*] m.p. 98°. This

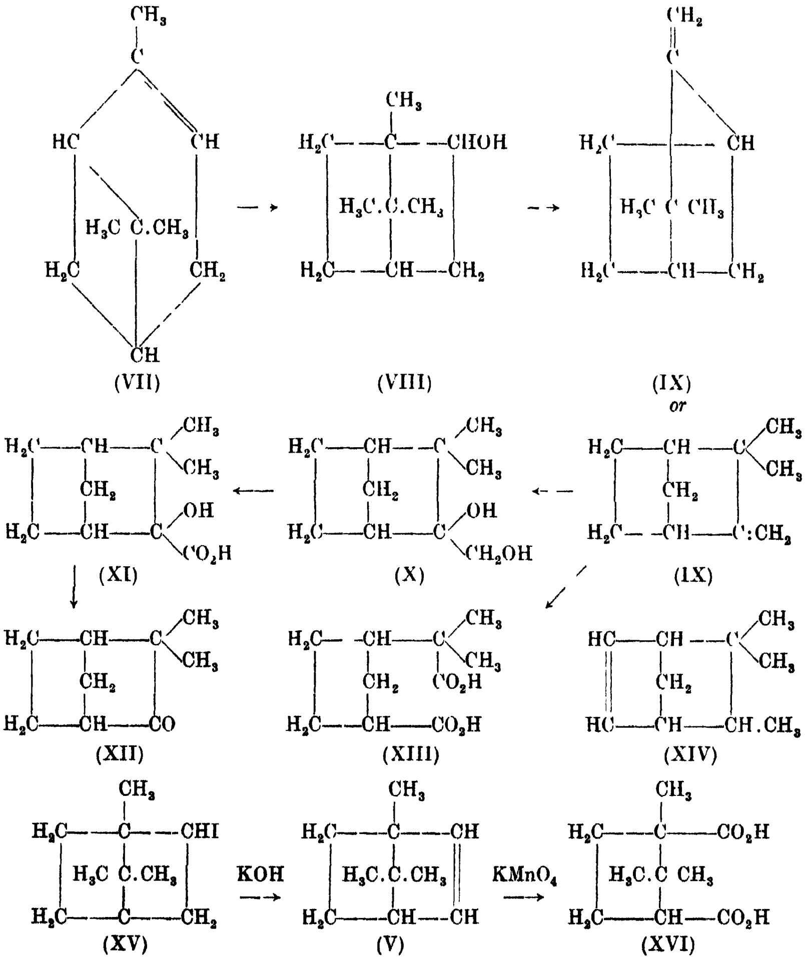
---

* *J. Russ. Phys. Chem. Soc.* 1896, **28**, 64; *Ber.* 1897, **29**, 124.

† *J. Russ. Phys. Chem. Soc.* 1899, **31**, 680.

‡ *Ber.* 1895, **28**, 1090. The Tiemann formula was based on his proposed modification of the Bredt camphor formula (see p. 376).

§ *Ibid.* 1899, **32**, 2302.

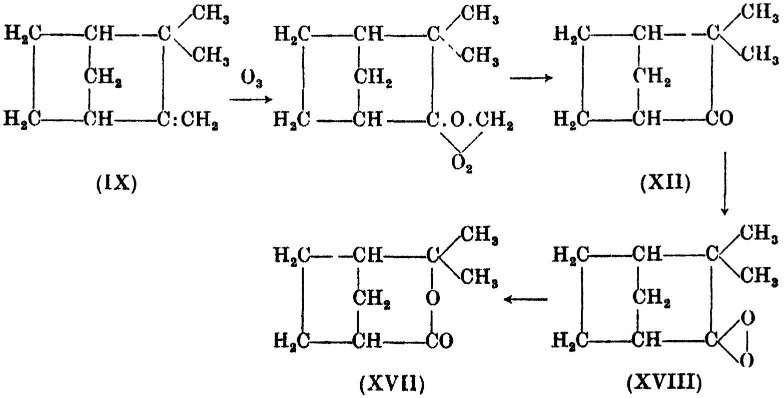


---

[*] Wagner and Brickner's bornylene was not quite pure and contained some tricyclene.

hydrocarbon must have the formula (V), previously assigned by Bredt to camphene, since on oxidation it gives *camphoric acid* (XVI). In this case the elimination of hydrogen iodide had taken place without intramolecular change.

Whilst the Wagner formula was successful in explaining in a simple manner the majority of the reactions of camphene, it did not readily account for its oxidation to camphenic acid with potassium permanganate or to *cis*-apocamphoric acid with nitric acid (see p. 301). What, however, appeared at first sight to be a more fundamental objection was the observation due to Semmler,* that on ozonolysis camphene did not yield, as would have been anticipated, *camphenilone* (XII) but the lactone, *dimethylnorcampholide* (XVII), the constitution of which was proved shortly afterwards by its synthesis.† An explanation of the formation of this lactone was, however, supplied by Harries and Palmén.‡ They found that, when camphene was ozonised in acetic acid solution and the ozonide decomposed in the usual manner, a mixture of approximately equal quantities of camphenilone (XII) and the lactone (XVII) was obtained. The latter was, however, a secondary product of the reaction resulting from the degradation of the ketone through the peroxide (XVIII), a reaction analogous to the oxidation by Caro's reagent of



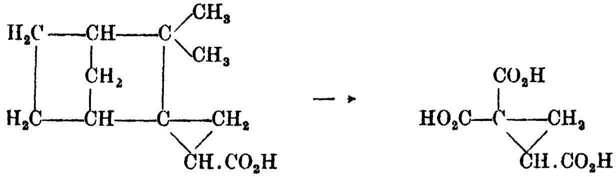
(IX) (XII) (XVII) (XVIII)

* *Ber.* 1909, 42, 246.

† Komppa and Hintikka, *Ber.* 1909, 42, 898.

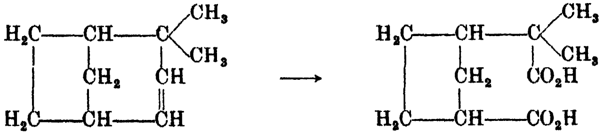
‡ *Ber.* 1910, 43, 1432.

saturated ring ketones to lactones.[*] Harries and Palmén concluded, therefore, that, contrary to the assumption of Semmler, the formation of the lactone was in full accord with the Wagner formula. This received additional support from the experiments of Buchner and Weigand,[†] who condensed camphene with ethyl diazoacetate and obtained an ester which gave on hydrolysis a tricyclic acid (XIX) and from the latter, by oxidation with potassium permanganate, cyclo*propane*-1:1:2-*tricarboxylic acid* (XX) was obtained. This acid could only result from the addition of the diazo-ester to an exocyclic ethylenic linkage, since, had this been endocyclic, *cyclo*propane-1:2:3-tricarboxylic acid would have been formed on oxidation.


(XIX) (XX)

These experiments of Buchner and Weigand were of considerable importance, since Aschan[‡] had shown that camphenic acid must have the constitution (XIII) suggested by Wagner. In his opinion the formation of camphenic acid was explained most simply if camphene was represented by the endocyclic formula (XXI).

This formula for camphene was, however, finally disproved by Lipp, Götzen and Reinartz's[§] synthesis of *endocamphene* (XXI) from *ω-bromocamphene* (XXII) (p. 288). When this bromide is treated with alkali it yields, amongst other products, a ketone, R-*homocamphenilone* (XXIII), *semicarbazone*, m.p. 210–211°, the


(XXI) (XIII)

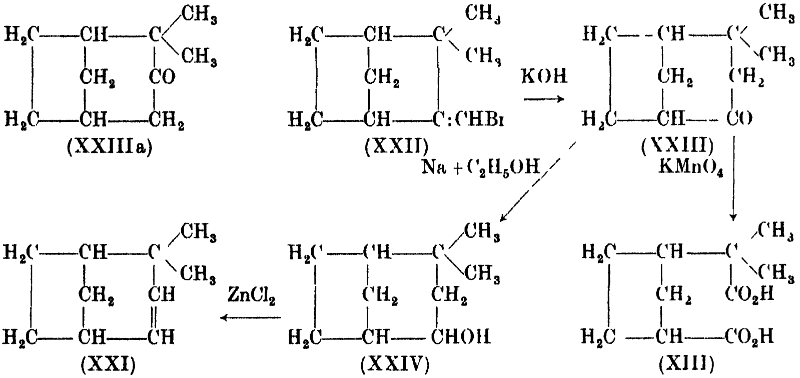
---

[*] Baeyer and Villiger, *Ber.* 1900, **33**, 858. [†] *Ber.* 1913, **46**, 759.

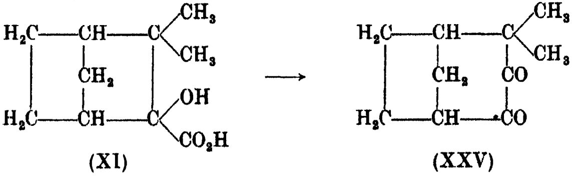
[‡] *Annalen*, 1910, **375**, 336. Aschan's proof of the constitution of this acid together with Lipp's synthesis is described on p. 299.

[§] *Ibid.* 1927, **453**, 1.

constitution of which was proved by its oxidation to camphenic acid (XIII) and by the fact that it was not acted upon by sodamide, which would have been the case if it had had the alternative formula (XXIIIa) (compare the action of sodamide on fenchone, p. 564). On reduction with sodium and alcohol R-*homocamphenilol* (XXIV), m.p. 73–76°, b.p. 107–110°/10 mm., *phenylurethane*, m.p. 119°, was obtained, which, by dehydration with zinc chloride in benzene solution, gave endocamphene (XXI), b.p. 170·6–171·6°/744·5 mm., $d_{4°}^{12·4°}$ 0·8957, $n_D^{12·4}$ 1·4844. The molecular refraction of endocamphene is normal and shows no exaltation, whereas that of camphene, in agreement with the presence of an exocyclic ethylenic linkage, has an exaltation of 0·51 unit.*



The conversion of the ω-bromide into the ketone involves a widening of the ring and has an analogy in the observations of Hintikka† that the lead salt of *camphenylic* acid (XI) on distillation yields *carbocamphenilone* (XXV), m.p. 58–59°, which, on oxidation with hydrogen peroxide, gave camphenic acid (XIII). A similar type of reaction is involved in the formation of carbofenchonone (p. 578).



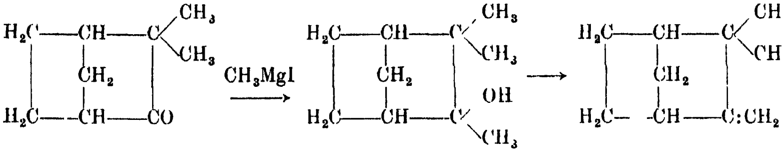
---

* Auwers, *Annalen*, 1912, 387, 240.

† *Ber*. 1914, 47, 512.

These experiments leave no doubt that Wagner's formula for camphene correctly represents the constitution of this hydrocarbon, and it is probable that the occurrence of camphenic acid amongst the oxidation products is due to the intermediate formation of carbocamphenilone by the action of alkali on camphenylic acid. This suggestion receives support from the observation of Langlois * that, if the oxidation is carried out in neutral solution, no camphenic acid is formed.

Camphene can be prepared by the dehydration of *methylcamphenilol* (XXVI) (p. 317), which is obtained by the action of methyl magnesium iodide on *camphenilone* (XII) and, since the latter has been prepared synthetically (see p. 368), this implies a complete synthesis of camphene.



(XII) (XXVI)

The dehydration of methylcamphenilol is best effected by warming with dilute sulphuric acid, and in view of the great tendency for camphene to isomerise in the presence of acids it would be dangerous, in the absence of other evidence, to accept this synthesis as a proof of the constitution of the hydrocarbon.

When camphene is present in an essential oil in quantity, it can readily be identified by separation in the crystalline form and determination of its melting-point, the identification being confirmed by hydration by the Bertram-Walbaum method to *iso*-borneol. When it is present in small percentages its recognition is not simple, and is probably best effected by its oxidation with potassium permanganate in acetic acid solution to camphenilone.

Somewhat divergent results have been quoted in the literature for the physical constants of camphene, but the following would appear to be representative values, the optically active and inactive modifications having approximately the same melting-point, 51–52°, b.p. 158·5–159·5°/760mm., $d_{4°}^{54°}$ 0·8422, $n_D^{54°}$ 1·5514, $[\alpha]_D$ $+103{\cdot}89°$, $-84{\cdot}9°$ (in ether), $+107{\cdot}7°$ (in benzene), $+99{\cdot}6°$

---

* *Ann. Chim.* 1919 [ix], **12**, 301.

(in alcohol). The hydrocarbon has probably not been prepared optically pure. The molecular refraction, 44·02, shows a marked exaltation, 0·51, over the calculated value, 43·51, in good agreement with the constitution assigned to the hydrocarbon.[*] The heat of combustion as determined by Auwers, Roth and Eisenlohr[†] is 1471 kg.-cals.

Before proceeding to a consideration of the properties of camphene, it may be useful to summarise the more important reactions by which it can be prepared. The majority of these originate from α-pinene[‡] and involve two Wagner rearrangements. The hydrocarbon can be prepared by the elimination of hydrogen chloride from bornyl chloride or from *iso*bornyl chloride; by the dehydration of borneol and *iso*borneol and by the action of acetic anhydride on bornylamine. By the use of suitable conditions it is possible to prepare by these methods camphene having a high rotatory power; thus *d*-bornyl chloride gives *l*-camphene, a reversal of sign occurring. Under many conditions, however, complete racemisation occurs, and it is only recently that a reasonable explanation of this inactivation has been put forward. It is necessary first to consider the work of Nametkin and Brüssoff[§] on the reactions of α-methylcamphene (XXVII), obtained by the dehydration of *tert.*-methylborneol (XXVIII) or of *tert.*-methylfenchyl alcohol (XXIX) (p. 291).[‖] On hydration, it does not give the expected 6-methyl*iso*borneol (XXX), which would be formed by a normal Wagner change, but the 4-*methyl* isomer (XXXI), which on dehydration gives a mixture of α- (XXVII) and β- (XXXII) methylcamphenes. The latter, on hydration, also gives 4-methyl*iso*borneol, but this can be explained by a normal Wagner rearrangement of the intermediate hydrate (XXXIII). In the case of α-methylcamphene, however, it appears that the primary hydrate (XXIX) first undergoes a pinacolic change into this β-methylcamphene hydrate (XXXIII). The fact that dehydration of the 4-methyl*iso*borneol gives both α- and β-methylcamphenes indicates the

---

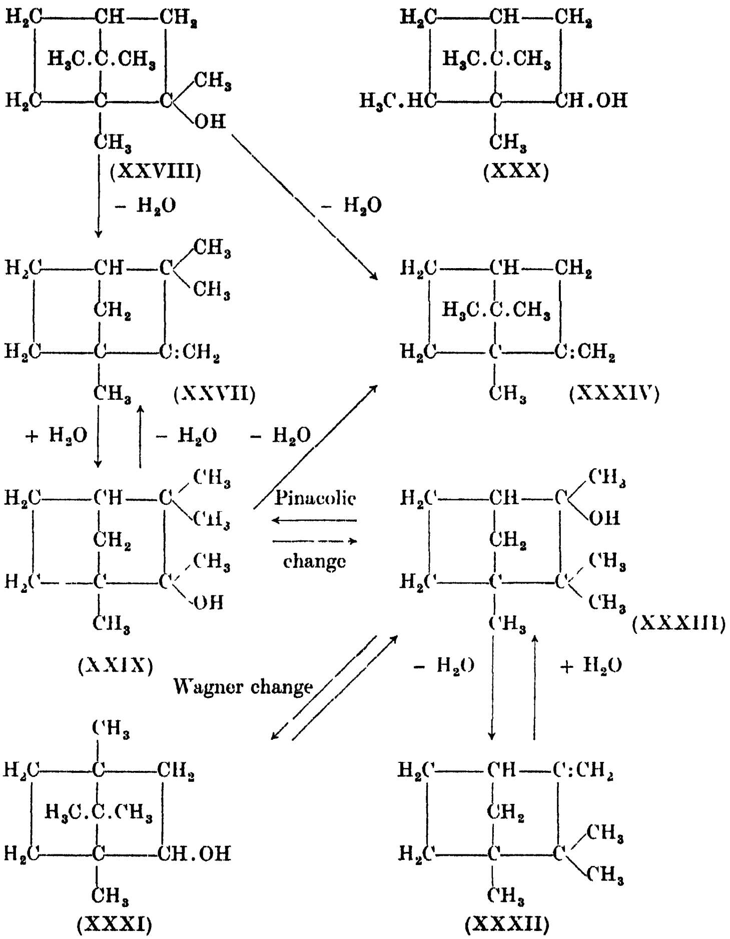
[*] Auwers, *Annalen*, 1912, **387**, 240.

[†] *Annalen*, 1910, **373**, 275; compare Roth and Östling, *Ber.* 1913, **46**, 323.

[‡] For the direct conversion of α-pinene into camphene, see p. 135.

[§] *Annalen*, 1927, **459**, 144; *J. pr. Chem.* 1932 [ii], **135**, 155; compare Bredt-Savelsberg and Buchkremer, *Ber.* 1931, **64**, 600; Schavrigin, *Chem. Abs.* 1948, p. 7276.

[‖] The α-methylcamphene is in each case accompanied by α-methylfenchene XXXIV).

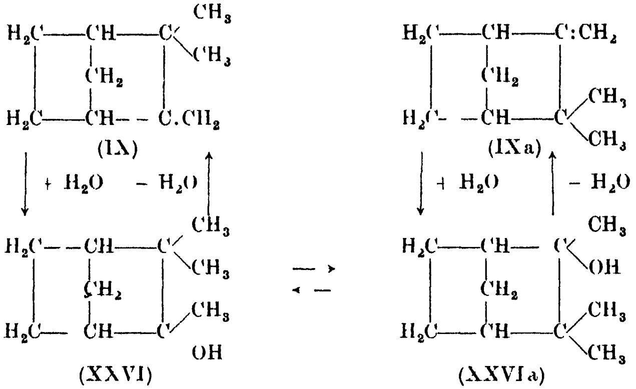


reversibility of the two reaction mechanisms. Similar transformations have been carried out on ethyl-, propyl-, and phenyl-*iso*borneols.*

Since in camphene itself (IX) the bridgeheads are identical, a similar series of transformations would not result in the formation of any structural isomers of camphene, but would give rise only to a change in configuration. Thus, in the scheme set out below, (XXVI) and (XXVIa) are not identical, but are mirror images, and it therefore follows that under conditions favourable to this pinacolic change, the product will be completely racemised.

---

* Nametkin *et al.*, *J. pr. Chem.* 1930 [ii], **124**, 144; *Ber.* 1933, **66**, 511; Sivkoff, *J. Gen. Chem. Russ.* 1945, **15**, 70.

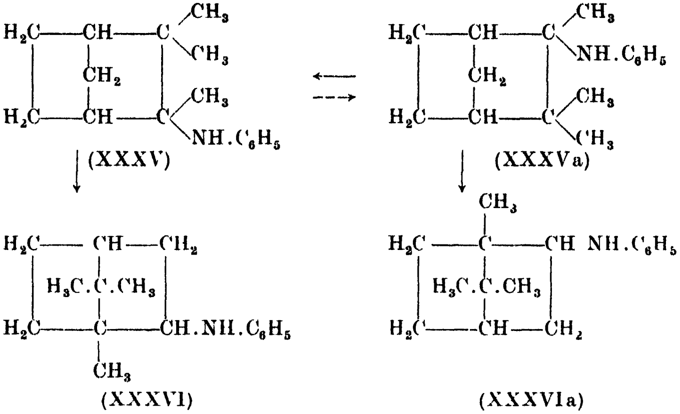


Similar considerations may be applied to the racemisation of camphene in non-aqueous solutions. Lipp and Stutzinger* have discussed the formation of camphene from bornyl chloride by the action of aniline, and conclude that the initial production of the hydrocarbon occurs through camphene hydrochloride. This primary camphene, however, which if isolated at this stage is optically active, reacts with aniline under the catalytic influence of the aniline hydrochloride already formed, to give the 2-derivative (XXXV). This may then undergo rearrangement to give iso*bornylaniline* (XXXVI), b.p. 173–175°/14 mm., $d^{18·5}$ 1·021, either by a direct Wagner change, in which case the product, if isolated without delay, shows $[\alpha]_D^{19·5°}$ −89·0°, or, if the reaction time is prolonged, by a transformation of the Nametkin type, via (XXXVa), to give a mixture of *d*- and *l*-forms (XXXVI) and (XXXVIa). The secondary camphene, obtained by thermal decomposition of the latter, will therefore be optically inactive.

The formation of optically active camphene from bornyl chloride by the use of other reagents, such as potassium phenoxide, is due to the inability of camphene to add the phenoxide

---

* *Ber.* 1932, **65**, 241; compare Houben and Pfankuch, *ibid.* p. 491; Nametkin and Schavrigin, *J. Gen. Chem. Russ.* 1934, **4**, 847; Kuwata, *J.S.C.I. Japan*, 1934, **37**, 389 B.



ion, and also to the fact that a certain degree of acidity is required for the pinacolic transformation to occur.

The inactivation of ω-substituted camphenes has been studied by Ritter and Vlases,[*] but the exact mechanism has not been established.

Camphene cannot be reduced with sodium and alcohol, whilst with hydriodic acid at 280° it yields a mixture of hydrocarbons which have not been identified. On catalytic hydrogenation it can, however, be readily reduced to *iso*camphane, the preparation and properties of which have already been discussed (p. 275). When the hydrocarbon is distilled over nickel in a current of hydrogen at 350–360° it yields *p*-cymene.[†]

Reference has already been made to the oxidation of camphene with ozone (p. 286). Autoxidation gives mainly camphenilone.[‡] By the action of perbenzoic acid, Faidutti[§] has prepared *camphene oxide* (XXXVII), b.p. 90–92°/20 mm., which on distillation with pumice yields *camphenilanaldehyde* (XXXVIII), m.p. 65–67°, b.p. 81–82°/10 mm. (*semicarbazone*, m.p. 191–192°); this isomerisation to the aldehyde is also catalysed by zinc bromide, so that the Reformatsky reaction, applied to the oxide, gives products identical with those which would be obtained from the aldehyde.[||] Camphenilanaldehyde is also formed, together with camphene glycol, by the oxidation of camphene with peracetic acid.[*] By the oxidation of camphene with hydrogen peroxide in acetic acid solution Henderson and Sutherland[†] obtained a number of products, the more important being (i) camphene glycol, (ii) camphenilone, (iii) iso*camphenilanaldehyde*, a stereoisomeride of camphenilanaldehyde (XXXVIII), (iv) *camphenanic acid*, $C_9H_{15}CO_2H$, and (v) a substance, $C_9H_{16}O_2$, b.p. 94–96°/14 mm., the constitution of which has not been determined; it had

---

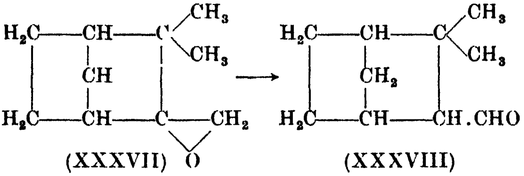
[*] *J. Amer. C.S.* 1942, **64**, 583.

[†] Sabatier and Gaudion, *Compt. rend.* 1919, **168**, 671.

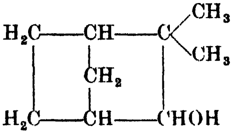
[‡] Dupont, *Ind. chim. Belg.* 1940 [ii], **11**, 3.

[§] *Compt. rend.* 1929, **189**, 854.

[||] Arbusov, *J. Gen. Chem. Russ.* 1939, **9**, 255.



(XXXVII) (XXXVIII)



(XXXIX)

somewhat curious properties since, whilst it gave camphenilone on oxidation with potassium permanganate, on treatment with phthalic anhydride it gave the *hydrogen phthalate*, m.p. 163-164°, of an alcohol, $C_9H_{16}O$, m.p. 94–95°, probably a stereoisomeric mixture of camphenilols (XXXIX) (see p. 369). In a subsequent communication, Henderson and Sutherland[‡] discussed the problem of the relationship of the various isomeric acids, $C_{10}H_{16}O_2$, derived from camphene, which have been described. These are four in number: (i) *camphenilanic acid*, m.p. 65°, prepared by Bredt and Jagelki[§] by the exposure of camphenilanaldehyde to the air; (ii) iso*camphenilanic acid*, m.p. 118°, which is formed when camphenilanic acid is repeatedly crystallised from water, alcohol or light petroleum, but not if acetic acid is used. It is also obtained when this acid is boiled for some time with dilute nitric acid and by the oxidation of either camphenilanaldehyde or *iso*camphenilanaldehyde with potassium permanganate; (iii) and (iv) camphenanic acid, m.p. 95°, and *iso*camphenanic acid, m.p. 74°, which result from the oxidation of either camphene or bornylene with hydrogen peroxide. These two acids have also been isolated by Aschan[‖] from amongst the products formed by the oxidation of camphene with potassium permanganate in acetic acid solution.

[*] Kumagae, *J.C.S. Japan*, 1944, **65**, 337.

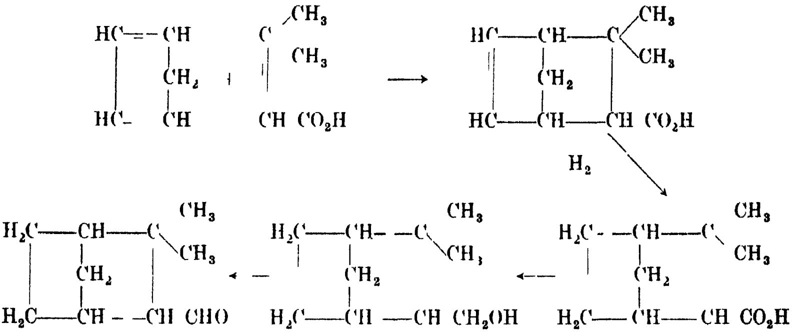
[†] *J.C.S.* 1911, **99**, 1539.

[‡] *Ibid.* 1914, **105**, 1710.

[§] *Annalen*, 1900, **310**, 112.

[‖] *Öfvers. Finska Vet. Soc.* 1911, **53 A**, no. 12.

According to Bredt[*] camphenilanic and *iso*camphenilanic acids are represented by (XL) and correspond to the two stereoisomeric forms of the aldehyde (XXXVIII). This structure has been confirmed for *iso*camphenilanic acid as a result of the work of Komppa and Komppa,[†] who have synthesised it by the hydrogenation of the condensation product from *cyclo*pentadiene and dimethylacrylic acid, as shown in the first part of the scheme below.



(XXXVIII) (XLI) (XL)

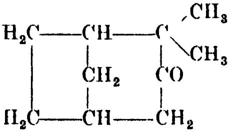
The relationship of camphenilanic and *iso*camphenilanic acids to the other two acids is obscure. Except *iso*camphenanic acid, the acids yield individual esters, b.p. 103-104°/22 mm., from which the original acids are obtainable on hydrolysis. From the ester prepared from *iso*camphenanic acid a mixture of camphenilanic and *iso*camphenilanic acids was obtained on hydrolysis. This can be interpreted in two ways. Either *iso*camphenanic acid is a mixture or else it isomerises on esterification. On reduction, all the esters were found to yield the same alcohol, *camphenilanol* (XLI), m.p. 77°, *hydrogen phthalate*, m.p. 153°, the constitution of which is proved by its oxidation to camphenilanaldehyde (XXXVIII). An alcohol of structure (XLI), m.p. 58-59°, had already been obtained by Semmler[‡] by reduction of the enol-acetate of camphenilanaldehyde; this is probably a stereoisomeric form.

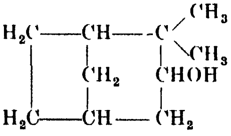
By oxidation of inactive camphene with lead tetra-acetate, Hückel and Kirschner[§] have obtained an *R*-homocamphenilone, m.p. 31°, $d_{4°}^{35°}$ 0·9727, $n_D^{35°}$ 1·4764 (*semicarbazone*, m.p. 223°; p-*nitrophenylhydrazone*, m.p. 187°), which they consider to have the structure (XXIII a). On reduction it gives two stereoisomeric forms of the corresponding R-*homocamphenilol* (XXIV a),[*] one of which has m.p. 84° (*hydrogen phthalate*, m.p. 139°; p-*nitrobenzoate*, m.p. 109°) and the other m.p. 101° (*hydrogen phthalate*, m.p. 144°; p-*nitrobenzoate*, m.p. 96°). Optically active forms of these alcohols, prepared from active camphene, have also been described; respectively they have m.p. 64°, $[\alpha]_D^{24°}$ + 8·4° in alcohol (3:5-*dinitrobenzoate*, m.p. 109·5°), and m.p. 68·5–70°, $[\alpha]_D^{21°}$ – 5·4° in alcohol (3:5-*dinitrobenzoate*, m.p. 99–101°).[†] On oxidation they give camphenic acid, and it is probable that *R*-homocamphenilone (XXIII a) is an intermediate in the formation of this acid by the direct oxidation of camphene. Reduction of the oxime of the *R*-homocamphenilone (XXIII a) gives two stereoisomeric R-*homoamino*iso*camphanes*, originally thought to be ω-amino*iso*camphanes.

---

[*] *Annalen*, 1909, **366**, 57. [†] *Ber.* 1936, **69**, 2606. [‡] *Ibid.* 1909, **42**, 964.

[§] *Chem. Ber.* 1947, **80**, 41; compare Ishidate, Inouye and Fukushima, *Bull. C.S. Japan*, 1942, **17**, 491.


(XXIII a)


(XXIV a)

The oxidation of camphene with chromic acid has been investigated by Berthelot,[‡] Riban,[§] Armstrong and Tilden[||] and by Kachler and Spitzer,[¶] and has been shown to yield amongst other products *camphor* (XLII). This oxidation obviously involves a Wagner rearrangement, and it seems probable that camphene hydrate (XXVI) is first formed which then tautomerises to borneol (or *iso*borneol) (VIII) (compare p. 355) and the latter is oxidised to the ketone. This method has been used for the manufacture of camphor, and yields up to 88 per cent. have been obtained in the presence of emulsifying agents such as naphthalenesulphonic acids.[*] By carrying out the oxidation in acetic anhydride-carbon tetrachloride solution, Treibs and Schmidt[†] obtained camphenilone, camphenilanaldehyde and camphenanic acid.

---

[*] It should be noted that the terms *R*-homocamphenilone and *R*-homocamphenilol are also applied to the structurally isomeric compounds (XXIII) and (XXIV) (p. 288).

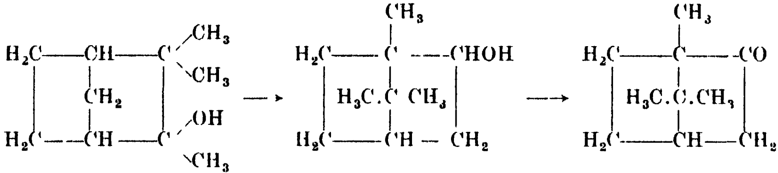
[†] These compounds were originally termed iso*camphanols* I and II, and were formulated as stereoisomeric forms of camphenilanol (Huckel *et al.*, *Ber.* 1937, **70**, 959; *Annalen*, 1941, **549**, 186.

[‡] *Compt. rend.* 1869, **68**, 334; *Annalen*, 1869, **150**, 374.

[§] *Ann. Chim.* 1875 [v], **6**, 387.

[||] *Ber.* 1879, **12**, 1756.

[¶] *Annalen*, 1880, **200**, 359.



(XXVI) (VIII) (XLII)

By the action of chromyl chloride on camphene Étard[‡] prepared an addition compound of the composition $C_{10}H_{16}, 2CrO_2Cl_2$, which was a light brown amorphous powder. It was extremely hydroscopic and was shown by Bredt and Jagelki[§] to be decomposed by water with the formation of *camphenilanaldehyde* (XXXVIII).

Brief mention has been made already (p. 284) of the more important products which result from the oxidation of camphene with potassium permanganate, a reaction which has been repeatedly studied since the pioneering investigation of Wagner.[‖]

By oxidation of the hydrocarbon dissolved in benzene with a 1 per cent. solution of potassium permanganate, Wagner obtained *campheneglycol* (X), m.p. 199·5–200°. The reactions of this glycol have been examined in some detail by Moycho and Zienkowski,[¶] who characterised it by the preparation of a *monobenzoate* (XLIII), m.p. 88°, from which by the action of phosphorus pentachloride they prepared the *enol-benzoate* (XLIV), m.p. 85–86°. When the latter was hydrolysed it gave *camphenilanaldehyde* (XXXVIII), which had been prepared previously by Milobendzki[**] from camphene glycol by the action of dilute acids.

If camphene glycol be further oxidised with potassium permanganate it yields *camphenylic acid* (XI), m.p. 170–172°, and *camphenilone* (XII), but no camphenic acid.

---

[*] Berlin, Davankov and Kalliopin, *J. Appl. Chem. Russ.* 1945, **18**, 217.

[†] *Ber.* 1928, **61**, 459.

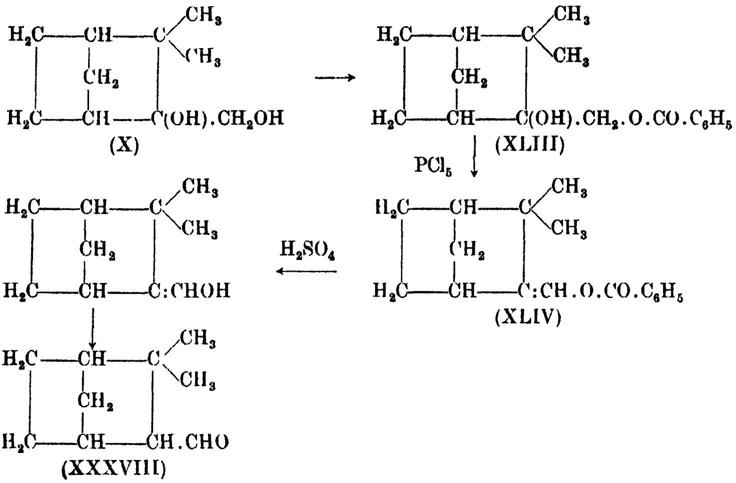
[‡] *Compt. rend.* 1893, **116**, 434.

[§] *Annalen*, 1900, **310**, 119.

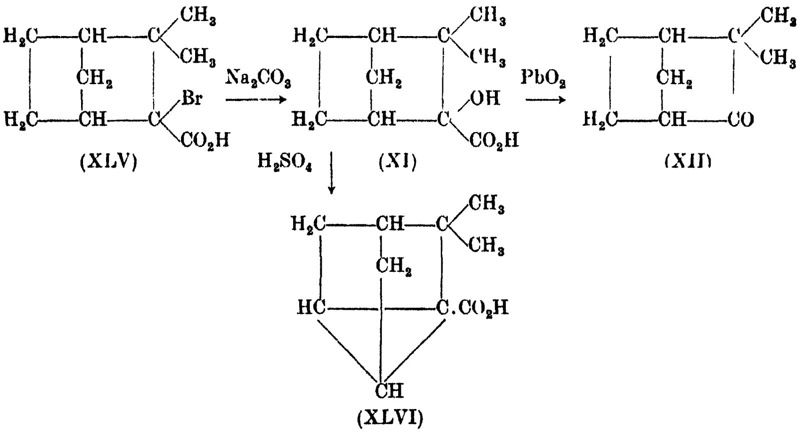
[‖] *Ber.* 1890, **23**, 2309.

[¶] *Annalen*, 1905, **340**, 17.

[**] *J. Russ. Phys. Chem. Soc.* 1899, **31**, 679.

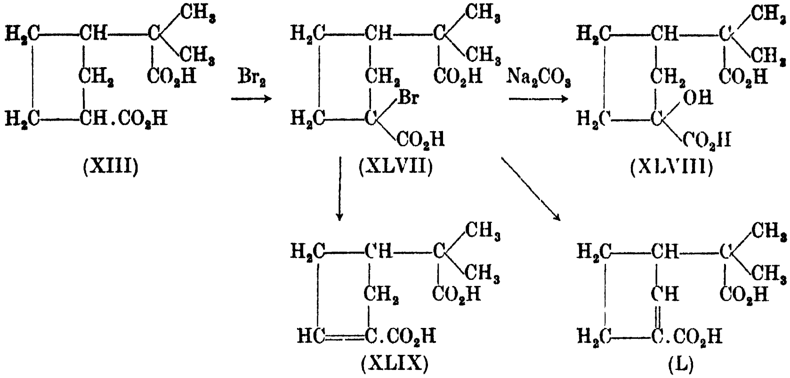


Camphenylic acid, which has been prepared also by the action of sodium carbonate on *bromocamphenilanic acid* (XLV),* has the usual properties of an α-hydroxy acid. It yields a sparingly soluble sodium salt and on further oxidation, with either lead peroxide or an acid solution of potassium permanganate, gives camphenilone. This ketone, together with *tricyclenic acid* (XLVI), is obtained also when the hydroxy acid is treated with concentrated sulphuric acid.



---

* Bredt and Jagelki, *Annalen*, 1900, **310**, 131.



When camphene is oxidised with potassium permanganate in alkaline solution, in addition to the products already mentioned, the dibasic acid, *camphenic acid*, is obtained. This acid, for which the following constants have been recorded by Aschan,* *cis-d-* and *l*-acids, m.p. 143·5–144·5°, $[\alpha]_D$ ± 18°, *cis-dl-*, m.p. 135·5–136·5°, *trans-*, m.p. 122–123°, has been shown by this author† to be represented by formula (XIII), as had been suggested originally by Wagner. By the action of bromine on the acid chloride a *bromocamphenic acid* (XLVII), m.p. 189–190°, was obtained, indicating that there was only one hydrogen atom in the α-position to the carboxyl groups. This acid gave on digestion with sodium carbonate solution *hydroxycamphenic acid* (XLVIII), m.p. 152°, and *dehydrocamphenic acid*, m.p. 155°, which from its method of preparation, assuming camphenic acid to have formula (XIII), must be represented by either (XLIX) or (L). For reasons which have already been given on p. 125 there can be no doubt that it has formula (XLIX).

Lipp,‡ by an ingenious synthesis shown schematically on p. 300, has proved conclusively the correctness of Wagner's formula for camphenic acid.

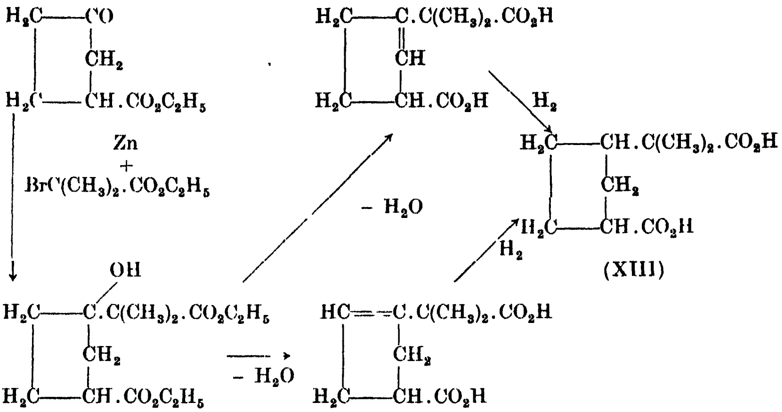
As has been mentioned already, the formation of camphenic acid in the oxidation of camphene is the result of an abnormal reaction. There can be no doubt that it is a secondary product formed by the action of alkali on camphenylic acid. Indirect evidence in support of this has been given by Langlois (p. 289)

---

* *Annalen*, 1911, **383**, 52.

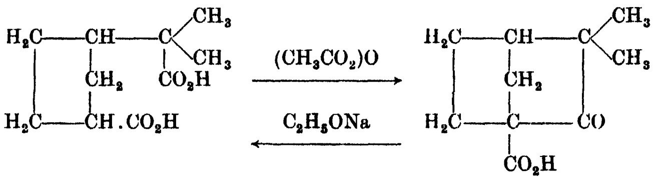
† *Ibid.* 1910, **375**, 336.

‡ *Ber.* 1914, **47**, 871.



and Hintikka (p. 288), whilst Aschan* has shown that when the hydroxy acid is fused with alkali camphenic acid is obtained.

Camphenic acid undergoes a number of interesting reactions. Reference is made on p. 368 to its conversion into camphenilone by the distillation of its lead salt. When the acid is heated with acetic anhydride, ring closure occurs with the formation of *camphenonic acid* (LI), *d*- and *l*-, m.p. 70°, *dl*-, m.p. 134°, which, although it is a β-ketonic acid, does not decompose on heating and in this respect resembles ketopinic acid (p. 301). When heated with sodium ethoxide at 180° it is reconverted into camphenic acid.†



(XIII) (LI)

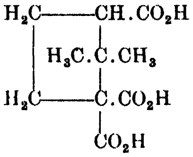
The oxidation of camphene with nitrogen peroxide gives camphenilone,‡ but nitric acid acts upon camphene both as a substituting and oxidising agent. It will be more convenient to consider here only the latter reaction, the former being discussed on p. 310. The oxidation of camphene with nitric acid was studied by Riban[*] and by Armstrong and Tilden,[†] but the first detailed investigation was due to Marsh and Gardner.[‡] They showed the main products of the reaction to be *carboxyapocamphoric acid* (LII), m.p. 199–200°, and *apocamphoric acid* (LIII), *cis*-, m.p. 203·5–204·5°, *anhydride*, m.p. 178–179°, *trans*-, m.p. 189–190°.

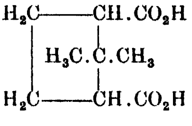
---

* *Ber.* 1914, **47**, 1121.

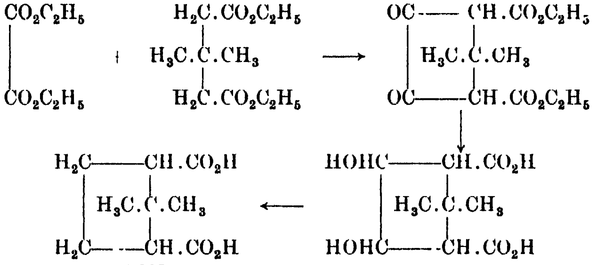
† Aschan, *Annalen*, 1915, **410**, 240; compare *Chem. Zentr.* 1935, II, 1556.

‡ Dulou, *Bull. Inst. Pin*, 1934, **54**, 135.


(LII)


(LIII)

The constitution of apocamphoric acid has been proved by its synthesis, for which we are indebted to Komppa.[§]


(LIII)

Carboxyapocamphoric acid loses carbon dioxide when it is heated above its melting-point and the third carboxyl group must therefore be attached to the same carbon atom as one of the other carboxyl groups. This only permits of it having formula (LII). It is obvious that in the course of the oxidation of camphene to apocamphoric acid a Wagner rearrangement must occur, and the mechanism of the reaction has formed the subject of considerable controversy. The position has, however, been clarified by the investigations of Komppa and his collaborators.[||] They found that, in addition to carboxyapocamphoric and apocamphoric acids, the ketonic acid, *ketopinic acid* (LVI), m.p. 234°, was also formed in the oxidation. This acid was first obtained by Armstrong, Gilles and Renwick[¶] by the oxidation of bornyl chloride with nitric acid. On fusion with potassium hydroxide or by heating with sodium oxide, it yields *pinophanic acid* (LV), m.p. 203°, the constitution of which is proved by its synthesis from *apocamphoric anhydride* (LIV) by the reactions outlined below.*

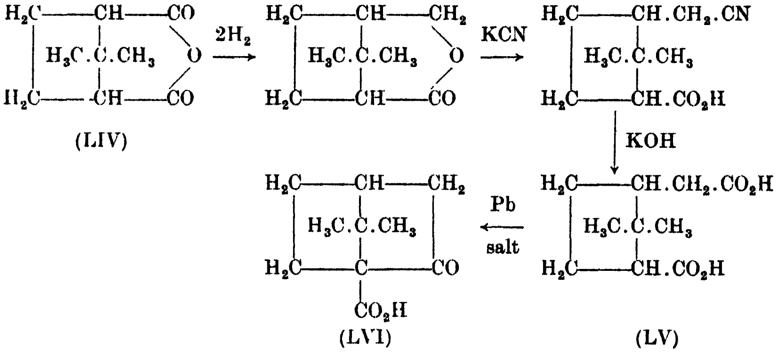
---

[*] *Ber.* 1878, **11**, 391. [†] *Ibid.* 1879, **12**, 1756. [‡] *J.C.S.* 1891, **59**, 648.

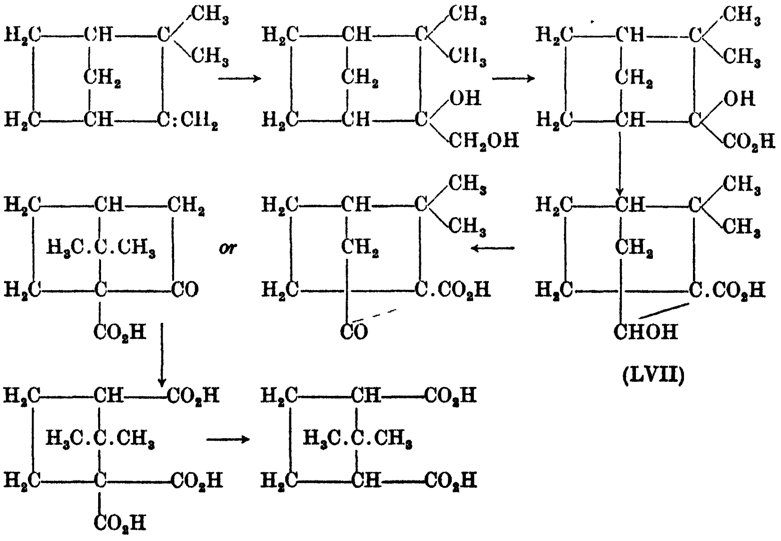
[§] *Ber.* 1901, **34**, 2472; *Annalen*, 1909, **368**, 126.

[||] *Ber.* 1908, **41**, 2747; 1911, **44**, 863, 1536; *Annalen*, 1909, **366**, 71.

[¶] *J.C.S.* 1896, **69**, 1401; Gilles and Renwick, *Proc. C.S.* 1897, **64**, 158.



The isolation of ketopinic acid makes it probable that the oxidation of camphene proceeds in accordance with the following scheme. All the substances shown, with the exception of the hydroxy acid (LVII), have been actually separated.



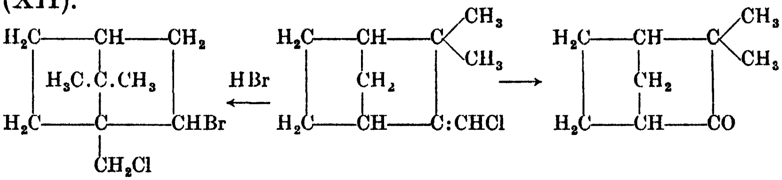
---

* Komppa, *Ber.* 1911, **44**, 1536.

Camphene does not undergo normal oxidation with selenium dioxide, but gives a *selenide*, $C_{20}H_{26}Se$, m.p. 93–94°, b.p. 220–225°/8 mm.[*]

Although camphene contains an ethylenic linkage, it does not react at all readily or smoothly with either chlorine or bromine. The early investigations of Marsh and Gardner[†] and of Semmler[‡] on the chlorination of the hydrocarbon left the nature of the products formed in a somewhat unsatisfactory position, which has, however, been clarified by the more recent investigations of Langlois[§] and of Meerwein and Wortmann.[||]

By the chlorination of camphene Langlois obtained an oil, b.p. 95–105°/10 mm., which, when boiled with dimethylaniline, gave pure *ω-chlorocamphene* (LVIII), b.p. 95–98°/15 mm., the constitution of which was proved by its oxidation to *camphenilone* (XII).



(LIX) (LVIII) (XII)

This chloride does not react with hydrogen chloride, but it gives on treatment with hydrogen bromide a crystalline *chlorobromocamphane*, m.p. 87–88°. This substance may have formula (LIX), but its constitution has not been definitely proved. It is also possible to prepare from ω-chlorocamphene a *trichloride*, $C_{10}H_{15}Cl_3$, m.p. 104°, which is probably also a camphane derivative, but the position of the chlorine atoms has not been determined.

Meerwein and Wortmann have described two isomeric chlorocamphenes. When *α-dichlorocamphane* (LX), prepared by the action of phosphorus pentachloride on camphor (see p. 433), is treated with potassium acetate in phenol solution it yields *α-chlorocamphene* (LXI) (p. 305), m.p. 20°, b.p. 193–197°, which on ozonolysis yields *α-chlorocamphenilone* (LXII), b.p. 116–118·5°/18 mm., *semicarbazone*, m.p. 206–207°.

---

[*] Zacharewicz, *Chem. Zentr.* 1936, II, 2384.

[†] *J.C.S.* 1897, 71, 289.

[‡] *Ber.* 1902, 35, 1021.

[§] *Ann. Chim.* 1919 [ix], 12, 193.

[||] *Annalen*, 1924, 435, 194.

When α-dichlorocamphane is treated in benzene solution with stannic chloride, it isomerises to *β-dichlorocamphane* (β-camphor dichloride), m.p. 178–179°, which, although originally considered by Meerwein and Wortmann to be a 2:6-dichlorocamphane, is now known to be 2:4-*dichlorocamphane* (4-*chloro*iso*bornyl* chloride) (LXIII).[*] When this substance is treated in phenolic solution with potassium acetate, it gives *β-chlorocamphene* (LXIV), m.p. 132–133°, b.p. 200°, which on ozonolysis yields *β-chloro*camphenilone (LXV), *semicarbazone*, m.p. 244–245°; at the same time some 4-*chlorotricyclene* (LXVI), m.p. 135–136°, is formed. It is clear, therefore, that the α-derivatives carry a chlorine atom on C_1, whilst in the β-derivatives the chlorine atom is on C_4. The isomerisation which occurs is evidently of the Nametkin type already discussed on p. 162, and according to Houben and Pfankuch[†] is best expressed in the scheme set out on p. 305, the pinacolic transformation of 1-chlorocamphene hydrochloride (LXVII) into the 4-chloro isomer (LXVIII) taking place under the catalytic influence of the stannic chloride.

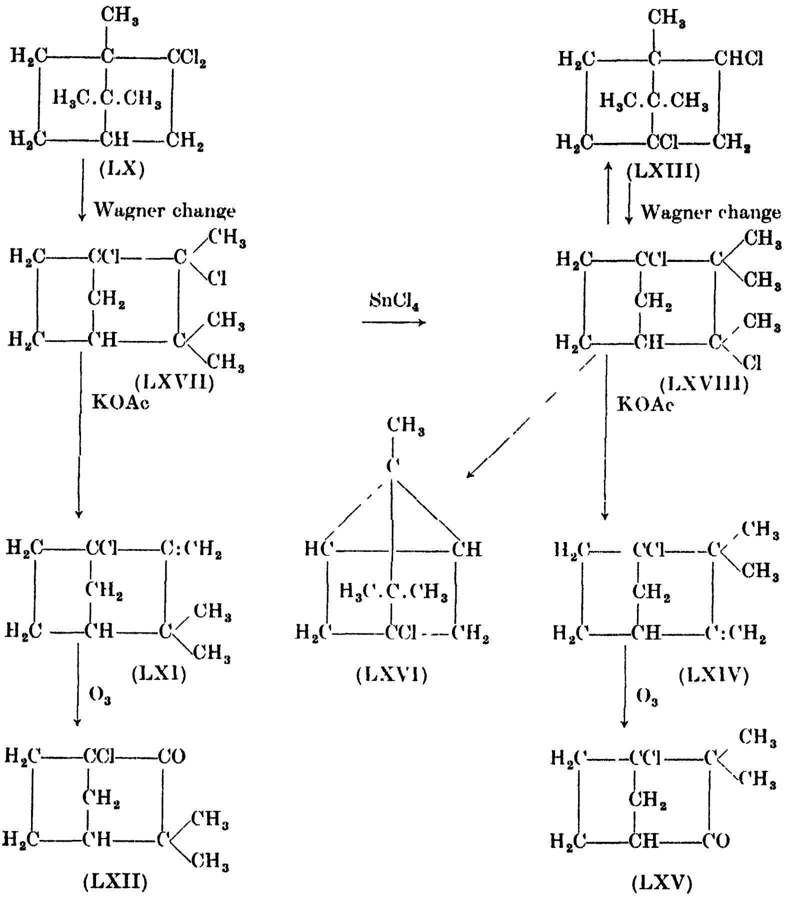
The conversion of 1-chlorocamphene into 4-chlorocamphene may also be brought about through the interconversion of the hydrobromides. When *l*-1-chlorocamphene (LXI), derived from *d*-camphor, is treated with hydrogen bromide, it gives a *hydrobromide*, m.p. 140–145°, $[\alpha]_D^{19°}$ $-11{\cdot}2°$ (in ether), which in *m*-cresol solution undergoes isomerisation to give 4-*chloro*iso*bornyl bromide*, m.p. 156–158°; treatment with pyridine then yields *l*-4-chlorocamphene (LXIV), m.p. 132–133°, $[\alpha]_D^{18°}$ $-108°$.

If the chlorine atom in either 1- or 4-chlorocamphene is replaced by hydrogen, camphene is formed, but since the 1:4-isomerisation brings about an inversion of the configuration of the molecule (compare p. 291), it would be expected that the products would be enantiomorphous. This is indeed the case, the camphene obtained showing $[\alpha]_D^{20°}$ $+97{\cdot}5°$ (from *l*-1-chlorocamphene, $[\alpha]_D$ $-12{\cdot}9°$) and $-105°$ (from *l*-4-chlorocamphene, $[\alpha]_D$ $-108°$), which confirms in a remarkable manner the reality of the Nametkin isomerisation. The extension of these reactions to the conversion of *d*- into *l*-camphor is considered on p. 522.

---

[*] Houben and Pfankuch, *Annalen*, 1931, **489**, 204.

[†] *Annalen*, 1933, **501**, 219.



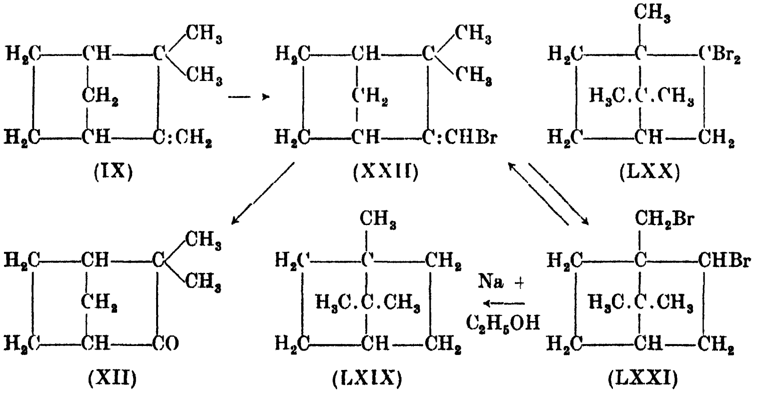
The bromination of camphene proceeds more smoothly than the chlorination, but the products have not been fully investigated. *ω-Bromocamphene* (XXII), which is an oil, was first described by Wallach,[*] who prepared it by the bromination of camphene in alcohol-ether solution, the bromination according to Reychler[†] proceeding more smoothly in light petroleum. ω-Bromocamphene is, however, not the sole product of the bromination, a not inconsiderable quantity of a dibromide being formed simultaneously. This dibromide, m.p. 90–91°, $[\alpha]_D^{20°}$ −71°

---

[*] *Annalen*, 1885, **230**, 235.

[†] *Ber.* 1896, **29**, 900.

(when prepared from *d*-camphene),[*] is also obtained when camphene hydrochloride[†] is brominated.[‡] The constitution of this dibromide has not been determined, but it must be a derivative of camphane (LXIX) and not of *iso*camphane, since Semmler[§] has found that, on reduction with sodium and alcohol, it gives the former hydrocarbon. For the dibromide Semmler tentatively suggested formula (LXX), whilst Langlois[‖] preferred (LXXI), which is probably correct. There would appear to be little doubt that the dibromide is not a direct product of the action of bromine on camphene, but is formed, as was first suggested by Marsh,[¶] by the action of hydrogen bromide on ω-bromocamphene.[**] The crystalline dibromide can be conveniently used for the preparation of ω-bromocamphene (XXII), since when digested with diethylaniline or quinoline it is converted into the latter, b.p. 115–120°/15 mm., $[\alpha]_D$ + 68·85°. The constitution of this bromide is proved by its conversion into camphene on reduction with sodium and alcohol[††] and by its oxidation with oxides of nitrogen to camphenilone (XII).[‡‡]



---

[*] Pariselle, *Compt. rend.* 1925, **180**, 1832.

[†] The camphene hydrochloride used by these authors was undoubtedly a mixture of bornyl chloride, *iso*bornyl chloride and camphene hydrochloride.

[‡] Junger and Klages, *Ber.* 1896, **29**, 544; Godlewski, *ibid.* 1899, **32**, 2303.

[§] *Ber.* 1900, **33**, 3425.

[‖] *Ann. Chim.* 1919 [ix], **12**, 193.

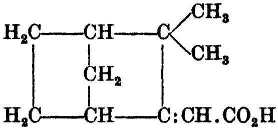
[¶] *Proc. C.S.* 1899, p. 54.

[**] For another view of the mechanism of the formation of the dibromide see Lipp, *J. pr. Chem.* 1922 [ii], **105**, 50.

[††] Semmler, *Ber.* 1900, **33**, 3425.

[‡‡] Langlois, *loc. cit.*

Langlois[*] investigated in some detail the reactions of ω-bromocamphene. When treated with hydrogen bromide it yields the dibromocamphane mentioned above, which on further bromination gives a *tribromide*, m.p. 77–78°, a substance first described by Semmler.[†] The position of the bromine atoms has not been determined. ω-Bromocamphene reacts readily with carbon dioxide in the presence of magnesium to give *camphene-ω-carboxylic acid* (LXXII), m.p. 124–125°, some hydrocarbon being produced simultaneously by the Wurtz reaction.



(LXXII)

Results of very great interest and importance have accrued from a study of the action of the halogen acids, more especially hydrochloric acid, on camphene. It was observed originally by Berthelot[‡] that camphene gave on treatment with hydrogen chloride a crystalline derivative, from which camphene could be regenerated by the action of alkali. This chloride, m.p. about 150°, was subsequently prepared by Riban[§] and by numerous other investigators,[‖] who showed it to be identical with *iso*bornyl chloride (LXXIII), its formation involving a Wagner rearrangement. A clear insight into the course of this reaction has resulted from the investigations of Aschan,[¶] supplemented by those of Meerwein and Emster.[**] Aschan found that when camphene was treated in methyl alcoholic or ethereal solution with hydrogen chloride the resulting product could be separated into two fractions, the first of which had m.p. about 150° and the second m.p. 125–127°, both of them being optically active in the opposite sense to the hydrocarbon from which they had been prepared and into which they could be reconverted by the action of alkali. According to Meerwein and Emster the higher melting of these hydrochlorides is somewhat impure *iso*bornyl chloride (LXXIII), whilst the lower melting is the true *camphene hydrochloride* (LXXIV),* which should exist in two stereoisomeric modifications (LXXIV) and (LXXIVa).

---

[*] Compare also Lipp, *J. pr. Chem.* 1922 [ii], **105**, 50; Lipp, Gotzen and Reinartz, *Annalen*, 1927, **453**, 1.

[†] *Ber.* 1902, **35**, 1020.

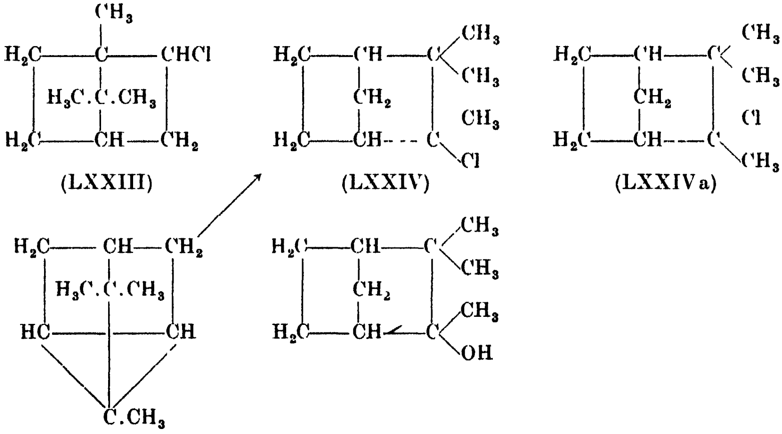
[‡] *Annalen*, 1859, **110**, 367.

[§] *Ann. Chim.* 1875 [v], **6**, 363, 372.

[‖] *Inter al.*, Kachler, *Ber.* 1878, **11**, 460; *Annalen*, 1879, **197**, 94; Spitzer, *ibid.* 129; 1880, **200**, 344; Jünger and Klages, *Ber.* 1896, **29**, 544; Reychler, *ibid.* p. 697.

[¶] *Annalen*, 1911, **383**, 7.

[**] *Ber.* 1920, **53**, 1815; 1922, **55**, 2500.



(LXXIII) (LXXIV) (LXXIVa)

(LXXV) (XXVI)

Camphene hydrochloride, which is extremely unstable, can also be prepared by the action of hydrogen chloride on *tricyclene* (LXXV). When kept at the ordinary temperature for some time camphene hydrochloride slowly isomerises, the reaction being catalysed by traces of acids, and passes into *iso*bornyl chloride. This change, however, is incomplete, since the reaction is reversible.† The chlorides can be readily distinguished and the percentage composition of a mixture be determined, since in solution camphene hydrochloride titrates like free hydrochloric acid. When shaken with water it passes smoothly into *camphene hydrate* (XXVI), which is also obtained when *iso*bornyl chloride is treated with milk of lime at 50–60°. Camphene hydrochloride on treatment with this reagent yields mainly camphene, very little of the hydrate being formed.

---

* These conclusions have been questioned by Aschan, *Naphtenverbindungen, Terpene und Campherarten*, 1929, pp. 177–183, but Meerwein and Emster would appear to be correct in their deduction.

† The transformation is discussed more fully on p. 347.

Semmler* attempted to prepare camphene hydrobromide by the action of hydrogen bromide on camphene, but obtained only *iso*bornyl bromide. More recently Meerwein, Hammel, Serini and Vorster† have found that, if hydrogen bromide is allowed to react with camphene in light petroleum solution, camphene hydrobromide is obtained together with some *iso*bornyl bromide. The hydrobromide has not been prepared in a pure state and is even more unstable than the hydrochloride, passing rapidly in the presence of traces of acids or moisture into *iso*bornyl bromide.

Camphene hydriodide has not been described, Kondakov and Lutschinin‡ having found that *iso*bornyl iodide is formed by the action of hydrogen iodide on the hydrocarbon.

The action of hypochlorous acid on camphene, first studied by Slawinski,§ has been shown by Henderson, Heilbron and Howie‖ to yield a *chlorohydrin*, $C_{10}H_{16}(OH)Cl$, m.p. 93°, which they regard as a chloro*iso*borneol, since, on reduction with zinc dust in alcoholic solution, it yields *iso*borneol. The constitution of this substance cannot, however, be considered to be established. On treatment with alkali it yields *iso*camphenilanaldehyde (XXXVIII), whilst on oxidation with chromic acid it gives a *chloroketone*, m.p. 132°, *oxime*, m.p. 142–143°, *semicarbazone*, m.p. 220–221°. This ketone, which gives camphor on reduction, is identical with that prepared in a similar manner from *bornylene chlorohydrin* (p. 330) which is considered to be a chloroborneol, since it gives on reduction borneol. Henderson and his collaborators apparently regarded camphene chlorohydrin and bornylene chlorohydrin as stereoisomerides having the formula (LXXVI), and, if this be the case, then the chloroketones should be identical with either α- or α′-chlorocamphor (LXXVII). The properties of the ketone differ, however, completely from those of the two α-chlorocamphors and agree more closely with those of ω-chlorocamphor (LXXIX), which according to Forster¶ melts at 132·5°, *oxime*, m.p. 134°.** If this identity should in the future be confirmed, then camphene chlorohydrin is probably a true camphene derivative having formula (LXXX), a constitution which would also account readily for its conversion into *iso*camphenilanaldehyde and *iso*borneol. It would be a structural isomeride and not a stereoisomeride of chlorohydrin (LXXVI) prepared from bornylene. This structure for camphene chlorohydrin* has been suggested by Detoeuf,† who prepared it by the action of monochlorocarbamide on the hydrocarbon. The alternative formula (LXXVIII) would appear to be extremely improbable, since a substance having this structure should resemble camphene hydrochloride in its properties.

---

* *Ber.* 1900, **33**, 3428.

† *Annalen*, 1927, **453**, 16.

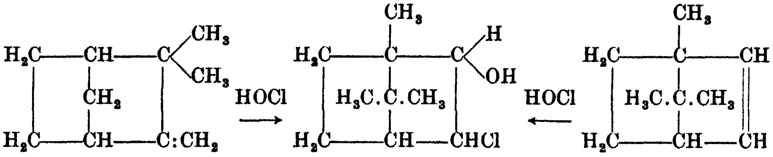
‡ *Chem.-Ztg.* 1901, **25**, 132.

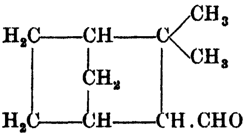
§ *Bull. Acad. Sci. Cracow*, 1905, p. 491.

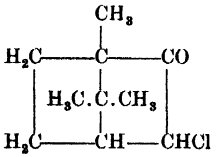
‖ *J.C.S.* 1914, **105**, 1367.

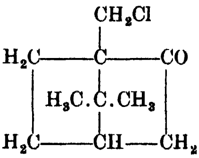
¶ *J.C.S.* 1902, **81**, 272.

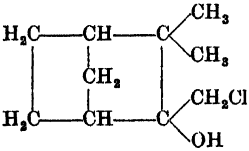
** The difference in the melting-points of the oximes may be due to that prepared from camphene hydrochloride being optically inactive. Henderson and his collaborators do not state if their preparations were optically active.

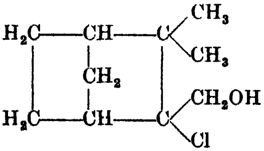

(LXXVI) (V)


(XXXVIII)


(LXXVII)


(LXXIX)


(LXXX)


(LXXVIII)

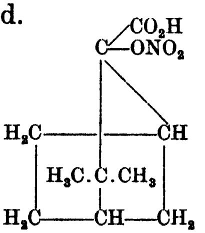
It was observed by Bouveault‡ that when camphene was treated with fuming nitric acid in chloroform solution two *camphene nitrates* were formed. One of these was unstable and decomposed on distillation in steam with regeneration of camphene, but the second volatilised without change and had the composition $C_{10}H_{16}$, HNO_3, and b.p. 110°/10 mm. It was decomposed by alkali with the formation of camphene. It is possible that these two nitrates are stereoisomeric camphene nitrates corresponding in constitution to camphene hydrochloride, but this has not been proved. By the action of nitrogen pentoxide on the hydrocarbon in chloroform solution, Demjanov[*] prepared a *nitro-acid*, $C_{10}H_{15}O_5N_3$, m.p. 140–141°, which doubtless has formula (LXXXI), since, on treatment with alkali or on reduction with zinc and hydrochloric acid, *tricyclenic acid* (XLVI) is obtained.

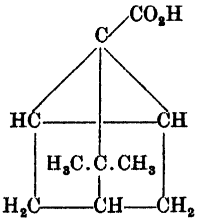
---

* A chlorohydrin possessing this constitution should be capable of existing in two stereoisomeric modifications.

† *Bull. Soc. chim.* 1922 [x], **31**, 179.

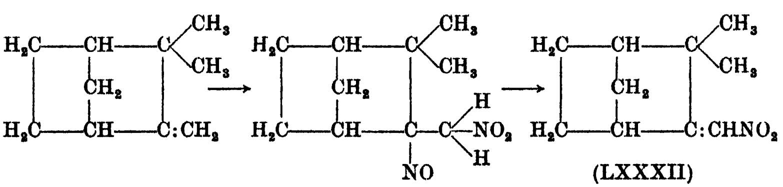
‡ *Ibid.* 1900 [iii], **23**, 537.


(LXXXI)


(XLVI)

During their investigation of the oxidation of camphene with dilute nitric acid, Marsh and Gardner[†] observed the formation of nitrocamphenes. These derivatives, which have been studied in greater detail by Jagelki[‡] and by Lipp,[§] can be prepared more conveniently by the action of oxides of nitrogen on camphene.[||] By the action of this reagent Jagelki prepared three substances, (i) *camphenilic nitrite*, (ii) *camphene nitrosite*, and (iii) *camphene nitronitrosite*.

Camphenilic nitrite, the *dl*-form of which melts at 64° and the active forms at 84–85°, $[\alpha]_D$ +153·4, −146·4° (in benzene solution), has been shown by Lipp to be *ω-nitrocamphene* (LXXXII), camphene behaving like *β*-pinene on nitration. According to Lipp, the nitration of camphene with oxides of nitrogen proceeds in accordance with the following scheme:


(LXXXII)

---

[*] *J. Russ. Phys. Chem. Soc.* 1901, **33**, 284.

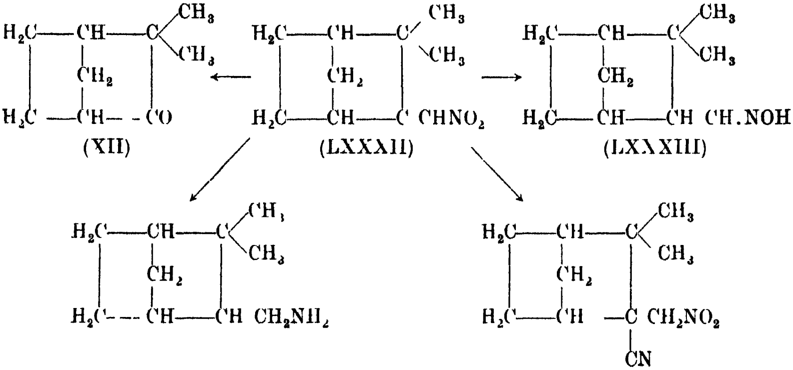
[†] *J.C.S.* 1891, **59**, 648; 1896, **69**, 74.

[‡] *Ber.* 1899, **32**, 1498.

[§] *Annalen*, 1911, **382**, 296; 1913, **399**, 241; 1914, **402**, 343.

[||] Blaise and Blanc, *Compt. rend.* 1899, **129**, 886; *Bull. Soc. chim.* 1900 [iii], **23**, 164; Komppa and Hintikka, *Annalen*, 1912, **387**, 294.

The constitution of ω-nitrocamphene was proved by its conversion (i) into camphenilone (XII) and potassium nitroacetate by the action of potassium hydroxide, (ii) into this ketone and nitromethane by the action of alcoholic ammonia, and (iii) by its reduction with aluminium amalgam to *camphenilanaldoxime* (LXXXIII). More recent investigations* have shown that on reduction with zinc and acetic acid it gives camphenilanaldehyde and tricyclal,† whilst with sodium and alcohol the main product is *ω-amino*iso*camphane* (LXXXIV). On treatment with sodium cyanide in alcohol, *nitro*iso*camphanyl cyanide* (LXXXV), m.p. 165–166°, $[\alpha]_D^{22°}$ +25° (in alcohol) is obtained. ω-Nitrocamphene is the most convenient source of camphenilone.



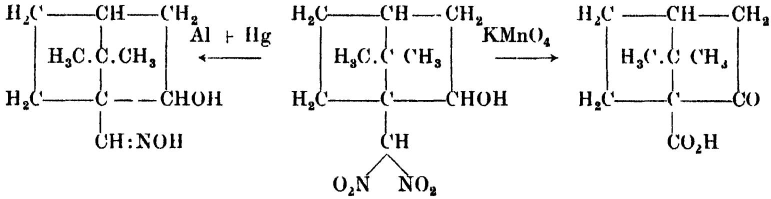
Camphene nitrosite, $C_{10}H_{16}O_5N_2$, m.p. 158·5°, can be purified through its sparingly soluble garnet-coloured potassium salt, m.p. 207–209°. It has been shown by Lipp to be *ωω-dinitro*-2-*hydroxycamphane* (LXXXVI), since on oxidation with potassium permanganate it yields *ketopinic acid* (LVI), whilst on reduction with aluminium amalgam it gives the *oxime* (LXXXVII).

The exact mechanism involved in the formation of this dinitrocamphane derivative from camphene has not been determined, since it is not formed by the action of nitric acid on ω-nitrocamphene. It is of interest, however, since it must be the parent substance of ketopinic acid, which is always obtained when camphene is treated with nitric acid.

---

* Lipp, Dessauer and Wolf, *Annalen*, 1936, **525**, 271; Lipp and Braucker, *Ber.* 1939, **72**, 2079; Lipp, Braucker and Sauer, *ibid.* 1940, **73**, 1146; Lipp and Mettegang, *ibid.* 1943, **76**, 1275.

† 2-*Acetoxyapocamphanealdehyde* is also formed in this reaction, its constitution being proved by conversion into ketopinic acid (LVI).



(LXXXVII) (LXXXVI) (LVI)

The constitution of camphene nitronitrosite, $C_{10}H_{15}O_5N_3$, has not been determined. It is a white powder decomposing at 149° and dissolving in nitrobenzene to give a blue solution.

In addition to ω-nitrocamphene two other nitrocamphenes have been described. In 1901 Forster[*] prepared a *nitrocamphene*, m.p. 56°, $[\alpha]_D$ +112° (in alcohol), by the action of silver nitrate on 2-*bromo*-2-*nitrocamphane* (LXXXVIII), which is formed when d-*camphoroxime* (LXXXIX) is treated with potassium hypobromite.[†] From its method of preparation and assuming that it is a nitrocamphene, although direct proof of this is lacking, Forster's nitrocamphene can have either structure (XC) or (XCI). Of these, (XCI) was suggested by Lipp[‡] and the fact that it is not identical with the α-nitrocamphene described below, to which this constitution must be assigned, was thought to be due to stereoisomerism. Later, however, Lipp and Lausberg[§] rejected this formula in favour of (XC), i.e. 1-*nitrocamphene*, which has also been accepted by Asahina and Yamaguti.[‖] The substance can be readily reduced with zinc dust in acetic acid solution to yield the corresponding 1-*aminocamphene*, m.p. 46°, b.p. 191–192°/758 mm., $[\alpha]_D$ +59·7° (in alcohol), from which by the action of nitrous acid a *hydroxycamphene*, m.p. 74°, is obtained. This alcohol on warming with dilute mineral acids is converted into camphor. It is of interest to note that this ketone is also obtained when 1-aminocamphene is warmed with acetic anhydride. When 1-nitrocamphene is treated with sulphuric acid in acetic acid solution, 4-*nitrocamphenehydrato-π-sulpholactone* (XCII), m.p. 133–134°, is obtained, the reaction being accompanied by a rearrangement similar to that observed with camphene itself (p. 316).

---

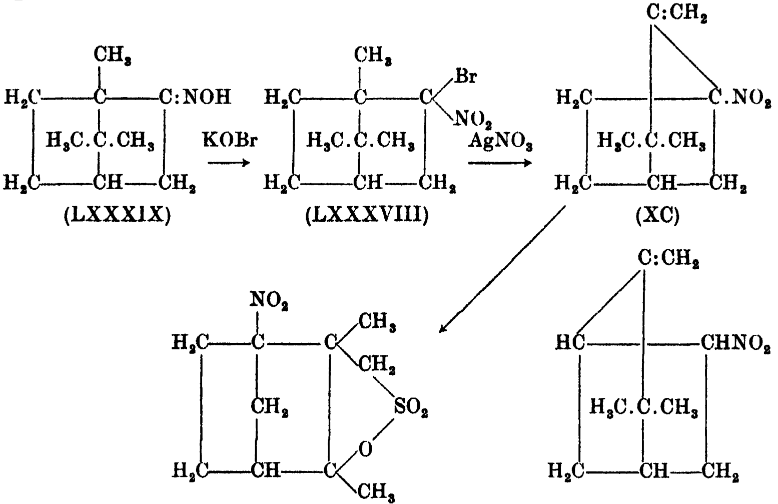
[*] *J.C.S.* 1901, **79**, 646.

[†] Forster, *J.C.S.* 1899, **75**, 1144.

[‡] *Annalen*, 1913, **399**, 241.

[§] *Ibid.* 1924, **436**, 279.

[‖] *Ber.* 1938, **71**, 318.



(LXXXIX) (LXXXVIII) (XC)

(XCII) (XCI)

α-Nitrocamphene (6-*nitrocamphene*), which must undoubtedly have formula (XCI), was prepared by Nametkin and Zabrodina* by the action of dilute nitric acid on *tricyclene* (LXXV). It is an oil, b.p. 119°/14 mm., $d_{4^\circ}^{20^\circ}$ 1·0689, $n_D^{20^\circ}$ 1·4942, and gives on reduction with zinc dust *α-aminocamphene* (XCIII), b.p. 197–198°/750 mm. From this base, after conversion into the quaternary *ammonium* derivative (XCIV), Nametkin and Zabrodina† prepared the hydrocarbon iso*camphodiene* or *camphinene* (XCV), m.p. 41·5–42°, b.p. 149–150°/763 mm., which yields on hydration an alcohol, *bornylenol*, m.p. 60–61°, b.p. 103–104°/10 mm., for which formula (XCVI) was suggested. More recently, however,‡ they have found that bornylenol is oxidised to a ketone, *tricyclenone*, m.p. 111–112°, the *semicarbazone* of which, m.p. 214–215°, is reduced by sodium ethoxide to tricyclene. It is possible, therefore, that bornylenol is actually a tricyclenol. It would thus be isomeric with ordinary tricyclol (p. 335). The same authors* have shown that the liquid α-nitrocamphene, on treatment with concentrated sodium hydroxide solution, is converted into the *aci*-form, α-iso*nitrosocamphene* (XCIa), m.p. 60–62°, which on treatment with aqueous methyl alcohol reverts to the nitro-form and yields the stereoisomeric α-nitrocamphene, m.p. 114–115°.

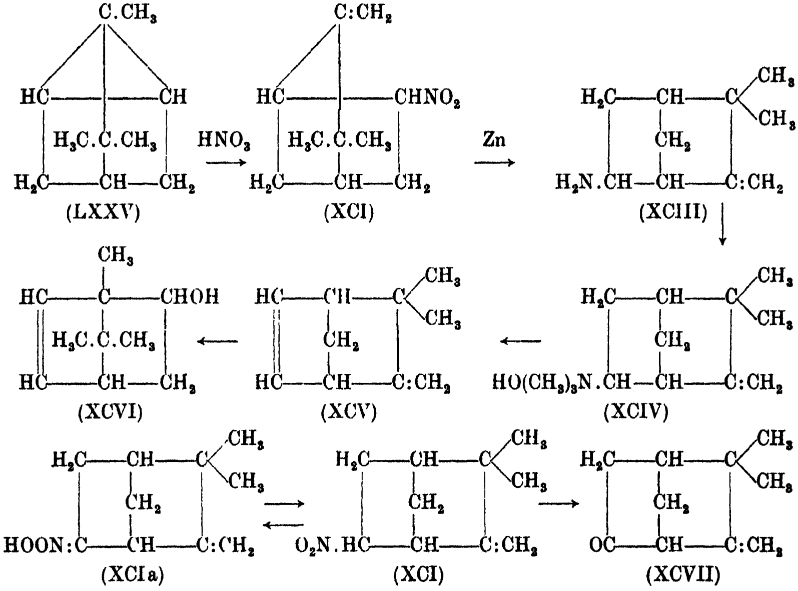
---

* *Annalen*, 1925, **441**, 181.

† *Ber.* 1928, **61**, 1491.

‡ *Compt. rend. Acad. Sci. U.R.S.S.* 1942, **36**, 142.

By the action of stannous chloride on α-nitrocamphene, Nametkin and Zabrodina† have prepared the ketone (XCVII), m.p. 77–78°, *semicarbazone*, m.p. 205°, *oxime*, m.p. 117–118°, which they designate *α-camphenone*.‡



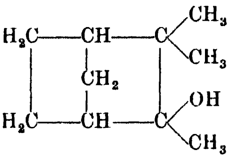
Much attention has been devoted to the study of the conditions governing the hydration of camphene. Assuming the reaction to proceed normally and without any molecular rearrangement, the tertiary alcohol, *camphene hydrate* (XXVI), should be formed. Whilst under suitable conditions this can actually be obtained as the main product of the reaction, under the conditions usually adopted for the hydration of hydrocarbons the secondary alcohol, iso*borneol* (VIII), is obtained. It was shown originally by Bertram and Walbaum[*] that when camphene was treated with a mixture of sulphuric and acetic acids *iso*bornyl acetate was obtained, Kachler and Spitzer[†] having previously prepared the corresponding alcohol by heating camphene with dilute sulphuric acid,

---

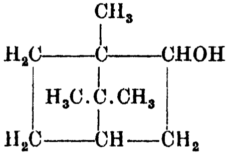
* *Bull. Acad. Sci. U.R.S.S.* 1937, p. 1015.

† *Ber.* 1926, **59**, 368.

‡ This name was applied originally to the ketone prepared by Angeli (*Gazzetta*, 1893, **23**, II, 351; 1894, **24**, II, 44, 317) from diazocamphor. This is now known (see p. 416) to be a tricyclic ketone (Bredt and Holz, *J. pr. Chem.* 1917 [ii], **95**, 133).



(XXVI)



(VIII)

and Wallach[‡] by the action of concentrated sulphuric acid. Many organic acids have been used as catalytic agents in carrying out this hydration, the corresponding *iso*bornyl esters being obtained, and, owing to its technical importance, the conditions governing the conversion have been very thoroughly investigated; many references to the subject will be found in the patent literature. If the reaction is carried out in alcoholic solution, then *iso*bornyl ethers are formed, as was first observed by Semmler.[§] Whilst *iso*borneol is always the main product of the hydration of camphene, Aschan[‖] showed that the stereoisomeric alcohol, borneol, was always formed simultaneously, the quantity varying with the conditions employed. When camphene is treated with sulphur trioxide in acetic acid solution, the main product, *iso*bornyl acetate, is accompanied by a crystalline lactone, m.p. 133°, which Lipp and Holl[¶] formulated as (XCVIII). Although they failed to oxidise it to camphor ω-sulphonic acid (XCIX) they observed that the lactone was formed by reduction of this sulphonic acid with sodium and alcohol to the hydroxy-acid (C) followed by dehydration, which appeared to confirm the postulated structure. More recently, however, Asahina, Sano and Mayekawa[**] have found that the lactone is formed in better yield from the hydroxy acid (CI) derived by reduction of camphor-π-sulphonic acid

[*] *J. pr. Chem.* 1894 [ii], **49**, 8.

[†] *Annalen,* 1880, **200**, 354.

[‡] *Ibid.* 1886, **230**, 235.

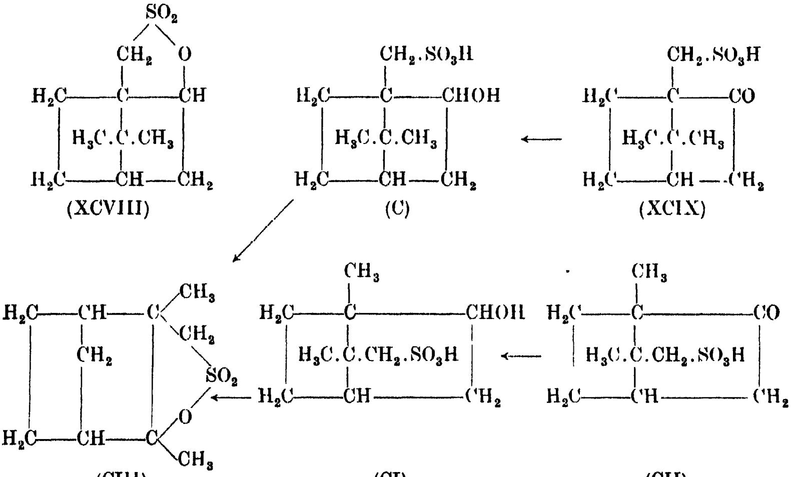
[§] *Ber.* 1900, **33**, 3430.

[‖] *Ibid.* 1907, **40**, 4923.

[¶] *Ibid.* 1929, **62**, 499.

[**] *Ibid.* 1938, **71**, 312.

(CII), and they conclude that it is more correctly represented as *camphenehydrato-π-sulpholactone* (CIII), formed from either sulphonic acid by rearrangement.



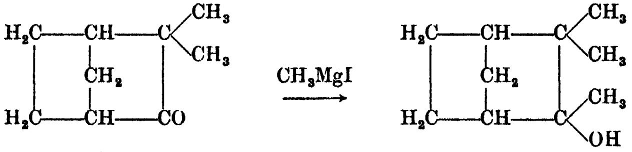
(XCVIII) (C) (XCIX) (CIII) (CI) (CII)

An alcohol having the structure of camphene hydrate (XXVI) was first prepared by Moycho and Zienkowski[*] by the action of methyl magnesium iodide on *camphenilone* (XII). *Methylcamphenilol* melted at 117–118° and gave a *phenylurethane*, m.p. 126°. From its method of preparation there was no doubt as to the constitution of this alcohol; on dehydration it could be converted readily into camphene, whilst when warmed with the Bertram-Walbaum hydrating mixture *iso*bornyl acetate was obtained. In 1908 Aschan[†] made the important observation that when camphene hydrochloride, or preferably bornyl chloride, was treated with milk of lime at 50–60°, or with dilute potassium hydroxide (4–6 per cent.), an alcohol was obtained which was undoubtedly *camphene hydrate*. This alcohol melted at 150–151°, b.p. 206–207·5°, phenylurethane, m.p. 89°, and when prepared from an optically active hydrocarbon was optically active (from *d*-camphene, $[\alpha]_D$ + 12·85°, camphene hydrate, $[\alpha]_D$ − 2·89°; from *d*-α-pinene, $[\alpha]_D$ + 38·4°, camphene hydrate, $[\alpha]_D$ − 21·79°). Camphene hydrate gives a p-*nitrobenzoate*, m.p. 96°, $[\alpha]_D$ − 32·6° (in benzene), a p-*benzamidobenzoate*, m.p. 129°, $[\alpha]_D$ −12·8° (in benzene), and a 3:5-*dinitrobenzoate*, m.p. 112°, $[\alpha]_D$ −24·9° (in alcohol), whilst methylcamphenilol gives a p-*nitrobenzoate*, m.p. 134–135°, $[\alpha]_D$ +40·3° (in benzene) (*dl*-form, m.p. 153°).* A prolonged study of the reactions of camphene hydrate and methylcamphenilol by Aschan† has shown conclusively that they are related to one another in the same manner as borneol and *iso*borneol and are in fact *cis-trans*-isomerides having the formulae (XXVIa) and (XXVIb).

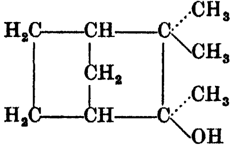
---

[*] *Annalen*, 1905, **340**, 58.

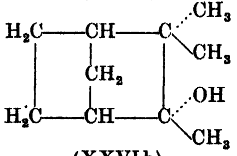
[†] *Ber.* 1908, **41**, 1092.



(XII) (XXVI)



(XXVIa)



(XXVIb)

If this be the case, then it would be anticipated that some camphene hydrate would be obtained by the action of methyl magnesium iodide on camphenilone. Although it has not proved possible to isolate pure camphene hydrate from this reaction, Aschan has obtained indirect evidence of its presence. Like borneol and *iso*borneol, camphene hydrate and methylcamphenilol show certain marked differences in their properties. If camphene hydrate be mixed with acetic acid, loss of water occurs immediately with the formation of camphene. The dehydration of methylcamphenilol is, however, much less rapid, but if crude methylcamphenilol, which has not been recrystallised, is mixed with acetic acid, owing to the presence of camphene hydrate the immediate formation of camphene can be observed. With the Bertram-Walbaum reagent both alcohols are converted into *iso*bornyl acetate, and by the action of hydrogen chloride they both yield camphene hydrochloride.

---

* Hückel, Doll, Eskola, Weidner, Neumann and Schneider, *Annalen*, 1941, **549**, 186.

† *Annalen*, 1911, **383**, 65; 1915, **410**, 222.

Whilst these experiments indicate that camphene hydrate is an intermediate product in the hydration of camphene to *iso*borneol (and borneol), more direct proof of this has been obtained by Aschan,[*] who made the important observation that when camphene was hydrated in ethereal solution with "diethyloxonium sulphate",[†] camphene hydrate containing only a small quantity of *iso*borneol was obtained. It is of interest to note that with "di-*iso*amyloxonium sulphate" the product is mainly *iso*borneol.[‡]

Meerwein and his collaborators[§] attempted to provide a theoretical explanation of the conversion of camphene hydrate into *iso*borneol and borneol, which owed its inception to their related work on the tautomerism of camphene hydrochloride, bornyl chloride and *iso*bornyl chloride. They concluded that camphene hydrate, borneol and *iso*borneol can be regarded as true tautomerides. It has already been mentioned (p. 308) that camphene hydrochloride is unstable and can be titrated in solution like free hydrochloric acid. If the hydrochloride be dissolved in methyl alcohol the percentage of hydrogen chloride falls gradually to a minimum and then once again rises to 100 per cent. An explanation of this somewhat remarkable observation is found in the occurrence of a series of reactions best illustrated by the scheme:

Camphene hydrochloride → camphene methyl ether → *iso*bornyl chloride
(A) (B) (C)
→ *iso*bornyl methyl ether
(D)

The change from (A) to (B) will occur with the liberation of hydrogen chloride, (B) to (C) with absorption of hydrogen chloride, whilst, in the final stage (C) to (D), hydrogen chloride will once more be liberated and be directly titratable. The correctness of this view of the mechanism of the reaction was proved by carrying out the first stage in the presence of potassium carbonate, when *camphene methyl ether* was obtained identical with that prepared by the interaction of the potassium derivative of camphene hydrate with methyl iodide. This ether, m.p. 12–14°, b.p. 201·5°, $[\alpha]_D$ −12·71° (from *d*-camphene, $[\alpha]_D$ +50·75°), when mixed with a methyl alcoholic solution of hydrogen chloride, passes into *iso*bornyl methyl ether (D), whilst if warmed with acetic acid it yields camphene.*

---

[*] *Medd. K. Vetenskaps-akad. Nobel-Inst.* 1919, **5**, no. 8, p. 19.

[†] This reagent is prepared by the interaction of monohydrate and ether.

[‡] Schwalbe and Aschan, *Finsk. Kem. Medd.* 1932, **40**, 133; **41**, 98.

[§] Meerwein and Gérard, *Annalen*, 1923, **435**, 174; Meerwein, Hammel, Serini and Vorster, *ibid.* 1927, **453**, 16.

Interesting results have been obtained also from a study of the hydration products of the esters resulting from the interaction of α-pinene and camphene with 2-chlorocymene-5-sulphonic acid and trichloroacetic acid. By the action of the former acid on α-pinene, *bornyl 2-chlorocymene-5-sulphonate*, m.p. 127-129°, is obtained, which passes on hydrolysis with alkali into a mixture of *iso*borneol, camphene hydrate and camphene. With camphene, on the other hand, iso*bornyl-2-chlorocymene-5-sulphonate* is formed together with a little of the bornyl ester, which on hydrolysis under similar conditions yields a mixture of *iso*borneol, camphene hydrate and camphene. Both esters behave therefore as if they were labile mixtures of all three alcohols. An analogous result was obtained when trichloroacetic acid was used. It was found, furthermore, that the tendency for the esters of camphene hydrate to pass into those of borneol and *iso*borneol was directly dependent upon the dielectric constant of the solvent in which the reaction was carried out, the velocity of the change increasing with the increase in this constant. This is in accord with the view that these intramolecular changes are ionic.

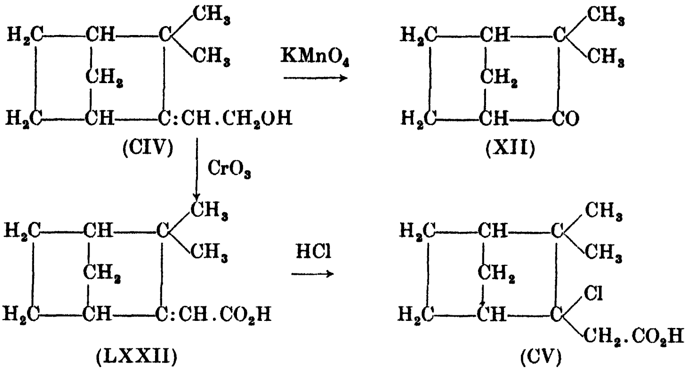
Camphene has been used in a number of synthetical investigations and reference may finally be made to some of these. When the hydrocarbon was heated with trioxymethylene in the presence of acetic acid it was found by Langlois† to give the alcohol (CIV), b.p. 125–126°/8 mm., d^{15° 0·987, $[\alpha]_D$ +45°, *hydrogen phthalate*, m.p. 124–125°. The constitution of this alcohol was proved by its oxidation with potassium permanganate to camphenilone (XII). By oxidation with chromic acid, it yields *camphene-ω-carboxylic acid* (LXXII), m.p. 124–125°, which readily loses carbon dioxide to give camphene. Of particular interest, however, is the observation of Langlois,‡ that the acid, when treated with hydrogen chloride, gave a stable *chloro-acid* (CV), m.p. 155–156°, which

---

* Camphere condenses with phenols at 0° to give *iso*bornyl ethers, which at higher temperatures rearrange to form nuclearly substituted phenols (Kitchen, *J. Amer. C.S.* **1948, 70, 3608**).

† *Ann. Chim.* **1919** [ix], **12, 193.**

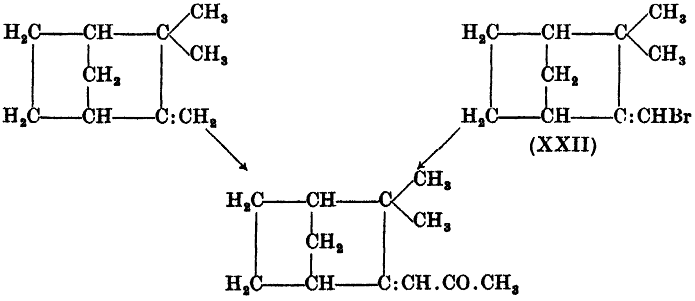
‡ *Bull. Soc. chim.* **1927** [iv], **41, 386.**



(CIV) (XII) (LXXII) (CV)

showed no tendency to undergo the Wagner rearrangement. This is due to the presence of the carboxyl group in the side chain, since in the case of the camphene-1-carboxylic acid prepared by Houben and his collaborators (p. 344) the intramolecular change readily occurs.

Lipp, Küppers and Holl* have found that camphene condenses readily with acetyl chloride in the presence of aluminium chloride to give *ω-acetylcamphene* (CVI), b.p. 112·6–114°/12 mm., $d_{4^\circ}^{11\cdot4^\circ}$ 0·9817, *semicarbazone*, m.p. 199–200·5°, which can be prepared also by the action of acetonitrile on ω-bromocamphene (XXII) in the presence of magnesium. The constitution of the ketone is proved by its oxidation to camphenilone.



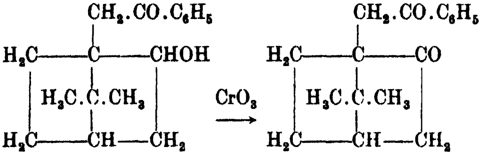
(XXII) (CVI)

With benzoyl chloride the reaction proceeds in a different manner, *ω-benzoylborneol* (CVII), m.p. 69–70°, being obtained, which gives on oxidation *ω-benzoylcamphor* (CVIII), m.p. 85–86°.

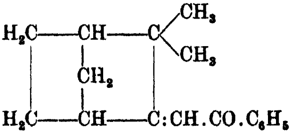
---

* *Ber.* 1927, **60**, 1575; Lipp and Quaedvlieg, *ibid.* 1929, **62**, 2311.

ω-Benzoylcamphene (CIX), b.p. 137–138·5°/0·7 mm., can, however, be prepared by the condensation of *ω*-bromocamphene with benzonitrile in the presence of magnesium, and also by the dehydration of *ω*-benzoylborneol.[*]



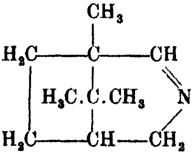
(CVII) (CVIII)



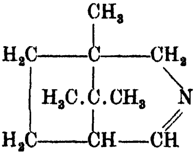
(CIX)

According to Kuwata,[†] a solution of camphene in benzene, when treated at 20° with an acid-earth catalyst, gives *dicamphene*, $C_{20}H_{32}$, b.p. 318–321°, d_4^{20} 0·9486, n_D^{20} 1·5090 (*hydrochloride*, m.p. 59°).

Camphene reacts with hydrazoic acid, undergoing ring enlargement, to give a mixture of α- (CX) and β- (CXI) N-*dehydrocamphidines*.[‡]

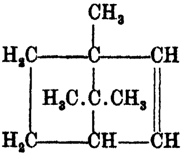


(CX)



(CXI)

BORNYLENE



The unsaturated hydrocarbon, *bornylene* (II), which has not been found to occur in nature, was first obtained in an impure state by Spitzer[§] by the treatment of 2:2-*dichlorocamphane* (I) with sodium.

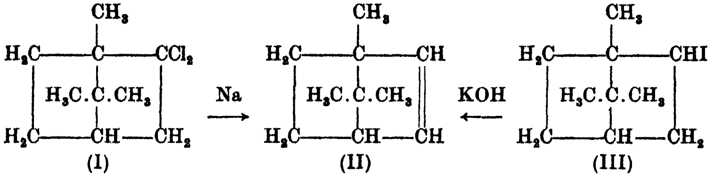
---

[*] Asahina and Sano, *Ber.* 1940, **73**, 747.

[†] *J.S.C.I. Japan*, 1933, **36**, 256 B.

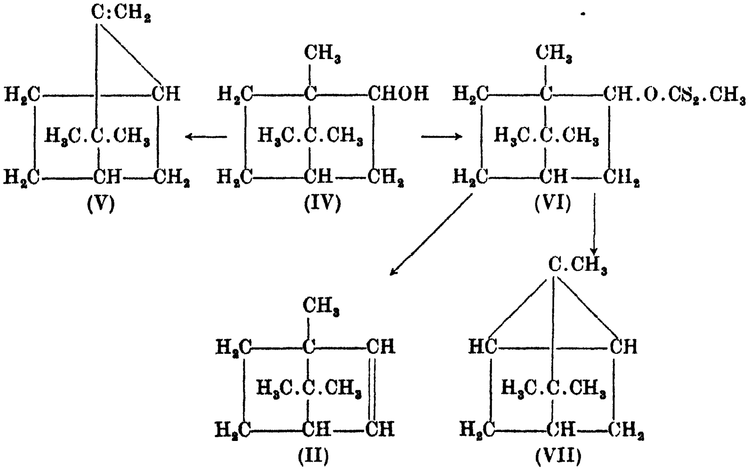
[‡] G.P. 583565.

[§] *Annalen*, 1879, **197**, 129.



In 1889, Wagner and Brickner* and Tschugaev† simultaneously described its preparation by two entirely different methods. During an investigation of the reactions of the bornyl halides the former found that, whilst *bornyl iodide* (III) on treatment with potassium phenoxide gave camphene, with a strong alcoholic solution of potassium hydroxide no molecular rearrangement occurred and bornylene was obtained. Meerwein and Joussen,‡ in the course of their interesting investigations on the tautomeric relationship of bornyl chloride, *iso*bornyl chloride and camphene hydrochloride, have studied in great detail the effect of the nature of the alkali, solvent and temperature on the reaction, and they have found that the bornyl halides can be converted by the action of potassium amyloxide at 190° into bornylene in a yield of 93 per cent.

As is described elsewhere, the dehydration of borneol and *iso*borneol (IV) leads by molecular rearrangement to *camphene* (V);



---

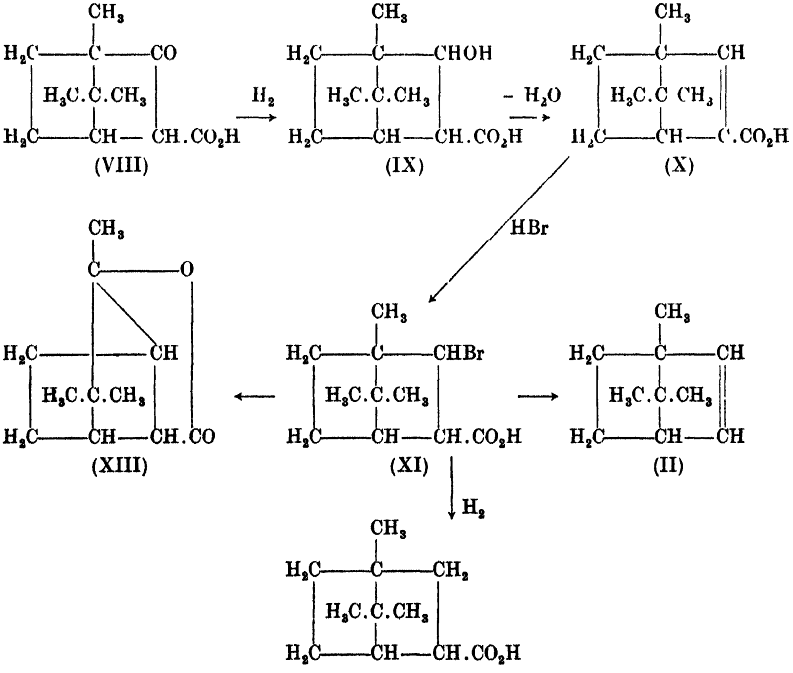
* *Ber.* 1900, **33**, 2121.

† *J. Russ. Phys. Chem. Soc.* 1900, **32**, 332.

‡ *Ber.* 1922, **55**, 2529.

it was found, however, by Tschugaev that if *methyl bornyl* (*iso*bornyl)-*xanthate* (VI) was distilled the decomposition proceeded normally with the formation of bornylene, the hydrocarbon having a rotation in the opposite sense to that of the alcohol from which it was prepared.

Bredt and his collaborators* have shown, however, that the bornylene prepared by this reaction is not pure, being contaminated with *tricyclene* (VII), from which it cannot be separated completely by crystallisation.† Pure bornylene was first prepared by Bredt by the following series of reactions. When d-*camphorcarboxylic acid* (VIII) (p. 451) is reduced electrolytically it yields d-*borneolcarboxylic acid* (IX), which gives on distillation d-*bornylene*-3-*carboxylic acid* (X), m.p. 112–113°. It was not found possible to eliminate carbon dioxide from this acid, but on treat-



---

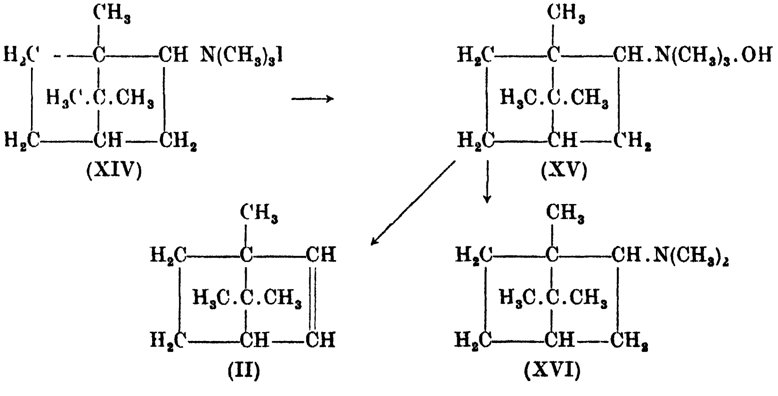
* Bredt and Sandkuhl, *Annalen*, 1909, **366**, 1; Bredt and Hilbing, *J. pr. Chem.* 1911 [ii], **84**, 778; Bredt, *ibid.* 1931 [ii], **131**, 137.

† Compare Tschugaev and Budrick, *Annalen*, 1912, **388**, 280.

ment with hydrogen bromide in acetic acid it gave d-2-*bromocamphane-3-carboxylic acid* (XI).[*] This reaction was shown to proceed without molecular rearrangement by reduction of the bromo-acid to d-*camphane-3-carboxylic acid* (XII). On warming the sodium salt of this acid, bornylene is obtained, but the yield is poor owing to the simultaneous formation of *γ-carboxylocamphenehydratolactone* (XIII), m.p. 183°, a Wagner rearrangement being involved in the formation of the lactone.

Whilst this method for the preparation of bornylene gives a very pure product, it is much more laborious than that of Tschugaev. It is therefore of interest to note that Henderson and Caw[†] found that it is possible to prepare the pure hydrocarbon by the xanthate process, if the crude hydrocarbon is carefully oxidised with hydrogen peroxide. It is somewhat remarkable that with this mild oxidising agent the tricyclic hydrocarbon should undergo preferential oxidation.

Another method for the preparation of pure bornylene has been devised by Ruzicka.[‡] *Bornyltrimethylammonium iodide* (XIV), m.p. 250°,[§] was converted into the hydroxide (XV), which, on distillation, gave a mixture of bornylene and *bornyldimethylamine* (XVI). This amine yields on treatment with methyl iodide an isomeric *trimethylammonium iodide*, m.p. 278–279°, possibly



---

[*] If *d*-bornylene-3-carboxylic acid is treated with hydrogen bromide in aqueous media an isomeric bromo-acid is obtained (see p. 451). It does not give camphane-3-carboxylic acid on reduction.

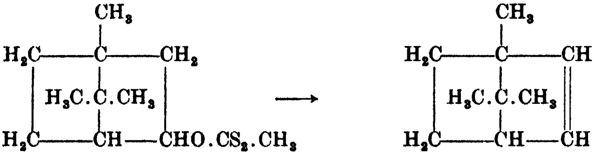
[†] *J.C.S.* 1912, **101**, 1416.

[‡] *Helv. Chim. Acta*, 1920, **3**, 748.

[§] Forster, *J.C.S.* 1899, **75**, 945.

*iso*bornyltrimethylammonium iodide, related to bornyltrimethylammonium iodide in the same manner as Forster's[*] bornylamine and *neoiso*bornylamine are related.

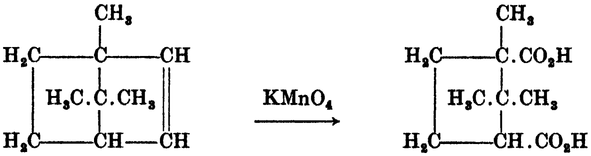
Bredt and Perkin[†] have shown that *l*-bornylene is obtained when *methyl* l-*epibornylxanthate* (XVII) is distilled. In this case there would appear to be no tendency for the formation of a tricyclic hydrocarbon to occur, since the *l*-bornylene was readily obtained quite pure.



(XVII) (II)

The formation of bornylene has been noticed in a number of other reactions. Thus Grignard, Bellet and Courtot[‡] found that it was formed when cyanogen was allowed to react with the product obtained by the action of magnesium on bornyl chloride, whilst Aschan[§] separated a small quantity as a by-product in the preparation of bornyl iodide by the action of iodine on bornyl chloride in the presence of magnesium. It has also been obtained by the action of sodium on 2:3-dichlorocamphane.[‖]

The constitution of bornylene follows from its oxidation to *camphoric acid* (XVIII), the camphoric acid being opposite in sign of rotation to that of the bornylene from which it is prepared.



(II) (XVIII)

Confirmation of the structure assigned to bornylene has been supplied by the work of Buchner and Weigand,[¶] who showed that on condensation with ethyl diazoacetate it yields a tricyclic *ester* (XIX), b.p. 135–138°/22 mm. The *acid*, m.p. 137°, prepared from this by hydrolysis, yields cyclo*propane*-1:2:3-*tricarboxylic acid* (XX) on oxidation.

---

[*] *J.C.S.* 1898, **73**, 386; 1899, **75**, 934; 1900, **77**, 1152.

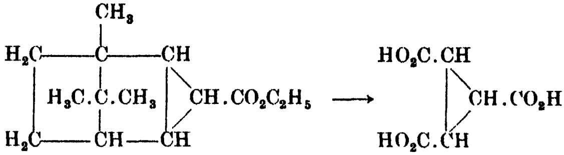
[†] *Ibid.* 1913, **103**, 2224.

[‡] *Ann. Chim.* 1919 [ix], **12**, 374.

[§] *Ber.* 1912, **45**, 2396.

[‖] Gandini, *Gazzetta*, 1936, **66**, 357.

[¶] *Ber.* 1913, **46**, 2108.

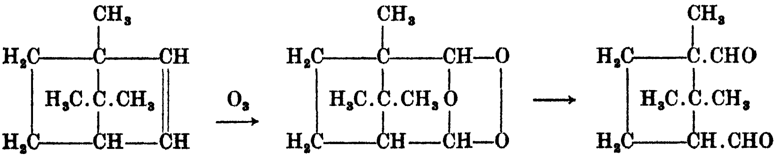


Bornylene is a crystalline solid, which is remarkably volatile. The following constants have been observed for the pure hydrocarbon prepared from *d*-camphor by Bredt's method: m.p. 113°, b.p. 146°, $[\alpha]_D$ $-21{\cdot}69°$ (in toluene, $c = 10{\cdot}45$). Tschugaev and Budrick[*] found the following values for *d*-bornylene: m.p. 109–109·5°, b.p. 146·5°/750 mm., $[\alpha]_D$ $+19{\cdot}29°$ (in toluene, $c = 12{\cdot}75$); from its melting-point it is doubtful if this specimen was quite pure. The specific rotations of *d*-bornylene in a number of different solvents have been recorded by McAlpine.[†] *dl*-Bornylene does not appear to have been described.

Bornylene can be most readily characterised by the preparation of its *nitrosite*, m.p. 163°, which was prepared by Henderson and Heilbron[‡] by the action of nitrous acid on the hydrocarbon.

By the catalytic hydrogenation of bornylene by the Sabatier-Senderens process using a nickel catalyst at 170–190°, Henderson and Pollock[§] obtained camphane.

On treatment with ozone in hexane solution, Harries and Haarmann[||] found bornylene to behave normally, yielding an *ozonide*, $C_{10}H_{16}O_3$ (XXI), which decomposed in acid solution to give a *dialdehyde*, b.p. 90–110°/16 mm. This dialdehyde probably has formula (XXII), but its characterisation and oxidation to camphoric acid do not appear to have been attempted.

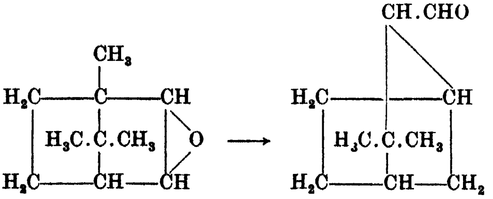


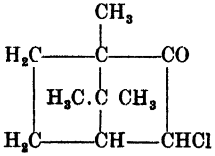
---

[*] *Annalen*, 1912, **388**, 288.
[†] *J.C.S.* 1932, p. 543.
[‡] *Ibid.* 1911, **99**, 1891.
[§] *Ibid.* 1910, **97**, 1621.
[||] *Ber.* 1913, **46**, 2595.

Although, as mentioned on p. 325, bornylene can be purified by oxidation of impurities with hydrogen peroxide, it is attacked by this reagent in acetic acid solution. The products of the oxidation have been investigated by Henderson and Caw.* They found the acids formed to consist of camphenanic and *iso*camphenanic acids and a *hydroxy*-acid, $C_8H_{12}(OH).CO_2H$. The constitution of the former acids is discussed on p. 295, whilst the constitution of the hydroxy-acid has not been determined. From amongst the neutral products, borneol, epiborneol and two glycols, $C_{10}H_{18}O_2$, m.p. 247–248° and 235–236°, were separated. The latter were not obtained in sufficient quantity for their constitution to be determined.

Bornylene was found by Henderson and Heilbron† to give, on oxidation with chromyl chloride, an additive compound, $C_{10}H_{16}$, $2CrO_2Cl_2$, isomeric with that obtained by the action of the same reagent on camphene (p. 297). By decomposition of this with water a number of substances were obtained, the principal product being *camphenilanaldehyde* (XXIV), which it is suggested is formed by a molecular rearrangement of the oxide (XXIII). In addition a *chloroketone*, $C_{10}H_{15}OCl$, m.p. 165°, *semicarbazone*, m.p. 234–235°, was obtained. This ketone gives on oxidation camphoric acid and, since it is not identical with either of the isomeric α-(or α′-)chlorocamphors (XXV), it is possibly a chloroepicamphor.


(XXIII) (XXIV)


(XXV)

Bornylene is readily oxidised by nitric acid to camphoric acid, but Henderson and Heilbron found that if a dilute solution of the mineral acid was used, 2:3-*dinitrocamphane* (XXVI), m.p. 137°, was also formed.

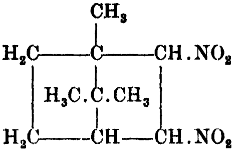
With chlorine, bornylene gives 2:3-*dichlorocamphane*, m.p. 126°.‡ By the action of hydrogen chloride on bornylene, Wagner

---

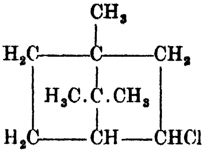
* *J.C.S.* 1913, 103, 1543.

† *Ibid.* 1911, 99, 1891.

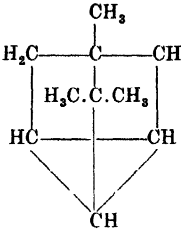
‡ Gandini, *Gazzetta*, 1936, 66, 357.



(XXVI)



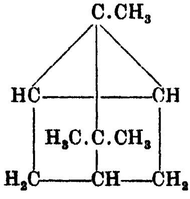
(XXVII)



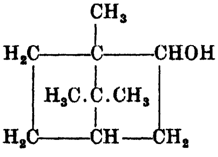
(XXVIII)

and Brickner* prepared a hydrochloride, *bornylene hydrochloride*, m.p. 138°. This hydrochloride must be 3-*chlorocamphane* (XXVII), since on treatment with potassium hydroxide at 140–150° under pressure it yields, in addition to camphene, iso*tricyclene* or *β-bornylene* (XXVIII), m.p. 117°, b.p. 150–151°/753 mm., which has also been termed iso*bornylene*. This hydrocarbon has been prepared by Bredt and Holz† from aminocamphor and from camphorquinonephenylhydrazone, and has been further studied by Nametkin and Brusova.‡

According to Achmatowicz,§ however, bornylene gives camphane derivatives having the halogen atom in position 2 when it is treated with the halogen acids. He has described a hydrochloride, m.p. 149–149·5°, $[\alpha]_D$ +15·43°, a *hydrobromide*, m.p. 124–125°, and a *hydroiodide*, m.p. 22–25°. These are stated to be intermediate between bornyl and *iso*bornyl halides in their reactivity and to yield, when heated with water at 100°, *tricyclene* (XXIX). On reduction with zinc dust they give camphene and by the action of silver acetate a new alcohol, *endoborneol*, m.p. 186° (*phenylurethane*, m.p. 138–139°). This alcohol is considered



(XXIX)



(XXX)

---

[*] *J. Russ. Phys. Chem. Soc.* 1903, **35**, 535.

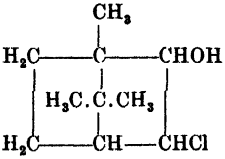
[†] *J. pr. Chem.* 1917 [ii], **95**, 133.

[‡] *J. Russ. Phys. Chem. Soc.* 1930, **62**, 333.

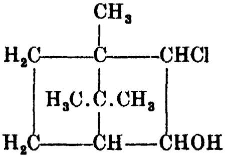
[§] *Rocz. Chem.* 1926, **6**, 804; 1928, **8**, 55; compare Krestinski and Eschtschenko, *J. Gen. Chem. Russ.* 1937, **7**, 415, 423.

to be stereoisomeric with borneol and *iso*borneol (XXX), but this would appear to be highly improbable since no other stable stereoisomers of the latter would be expected to exist. Adequate proof of the structure of these camphane derivatives is not available and a further study of them is desirable.

By the action of hypochlorous acid on bornylene, Henderson and Mair[*] have prepared a *bornylene chlorohydrin*, m.p. 99–101°, together with a *chlorocamphane*, m.p. 71–73°. The latter, which was not orientated, evidently owed its formation to the presence of hydrogen chloride in the hypochlorous acid used. Assuming no molecular rearrangement to have occurred, the chlorohydrin must be represented by either (XXXI) or (XXXII), and the former would appear to be the more probable, since on reduction with zinc dust borneol is obtained. This constitution cannot, however, be regarded as established, since on oxidation a chloroketone is formed identical with that prepared by the oxidation of camphene chlorohydrin. As mentioned on p. 309, this ketone agrees most closely in its properties with ω-chlorocamphor and further work is therefore necessary before the constitution of bornylene chlorohydrin can be regarded as proved. When it is treated with alkali it gives a small quantity of a *glycol*, m.p. 103–105°, possibly a stereoisomeride of camphor glycol (2:3-dihydroxycamphane), which melts at 230–231°.



(XXXI)



(XXXII)

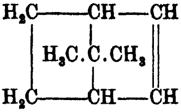
On hydration by the Bertram-Walbaum method, bornylene gives a mixture of bornyl and *iso*bornyl acetates, but the reaction proceeds much more slowly than in the case of camphene. It may be mentioned that Wagner and Brickner,[†] who first studied this reaction, considered that epiborneol was formed (compare p. 513).

---

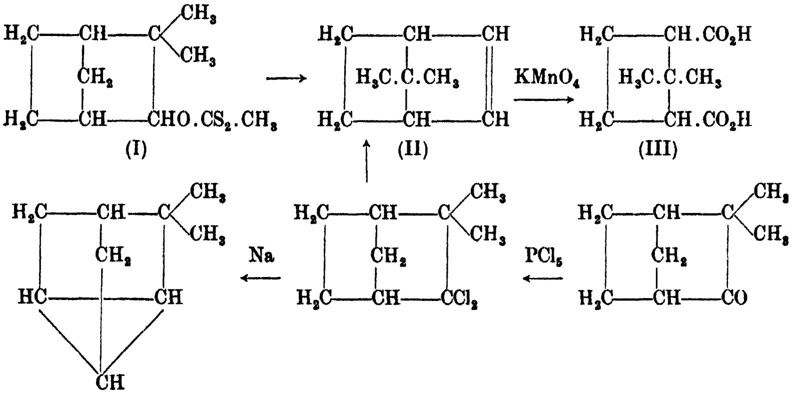
[*] *J.C.S.* 1923, **123**, 1155.

[†] *Ber.* 1903, **36**, 4602.

APOBORNYLENE



The hydrocarbon, *apobornylene* (II), C_9H_{14}, was first prepared by Wagner and Lemischewski[*] by the distillation of *methyl camphenilylxanthate* (I), and its constitution was proved by its oxidation with potassium permanganate to cis-*apocamphoric acid* (III), m.p. 205–206°, an acid which has been prepared synthetically by Komppa.[†] It will be observed that the conversion of the xanthate into the hydrocarbon involves a Wagner rearrangement.



Shortly afterwards, Moycho and Zienkowski[‡] showed that the *dichloride* (V), which could be prepared by the action of phosphorus pentachloride on *camphenilone* (IV), gave on reduction with sodium in ethereal solution apobornylene. A more recent study by Komppa and Roschier[§] of these methods for the preparation of apobornylene has shown that the hydrocarbon is not homogeneous, a stable saturated tricyclic hydrocarbon, *apocyclene* (VI), m.p. 42·5–43°, b.p. 138–139°/764 mm., $d_{4^\circ}^{40^\circ}$ 0·8710,

---

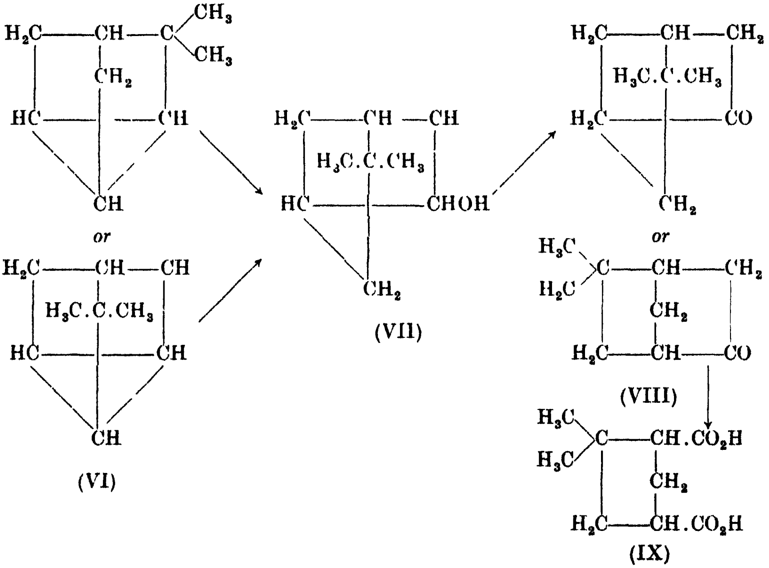
[*] Beilstein, *Handbuch der Organischen Chemie*, 4th ed. **5**, 123.

[†] *Annalen*, 1909, **368**, 126.

[‡] *Ibid.* 1905, **340**, 57.

[§] *Ibid.* 1922, **429**, 175; compare Hintikka and Komppa, *ibid.* 1912, **387**, 293.

$n_D^{40°}$ 1·4314, being formed simultaneously. In the formation of this latter hydrocarbon ring closure occurs without any molecular rearrangement. Nametkin and Alexandrov* have found that apocyclene can be most conveniently prepared by the action of mercuric oxide on camphenilone hydrazone in the presence of alkali.† Apocyclene can readily be obtained pure and free from apobornylene, since it is extremely resistant to the action of oxidising agents. Its constitution has been proved by its hydration to *β-fenchocamphorol* (VII), which was identified by oxidation to *β-fenchocamphorone* (VIII) and *apofenchocamphoric acid* (IX), m.p. 144–145°.‡



Apobornylene has m.p. 35·5–36°, b.p. 136–137°/755 mm., and has an odour resembling that of camphene. No crystalline derivatives have been prepared, but it can be readily identified by oxidation with potassium permanganate to *cis*-apocamphoric acid. On oxidation with ozone it yields a dialdehyde, but this cannot be purified and is rapidly oxidised by the air to apocamphoric acid.

---

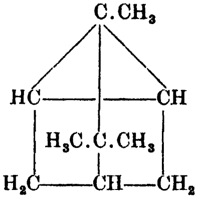
* *Annalen*, 1928, **467**, 191.

† Compare Meerwein and van Emster, *Ber.* 1920, **53**, 1815; Nametkin and Bogaheva, *J. Russ. Phys. Chem. Soc.* 1930, **62**, 1335.

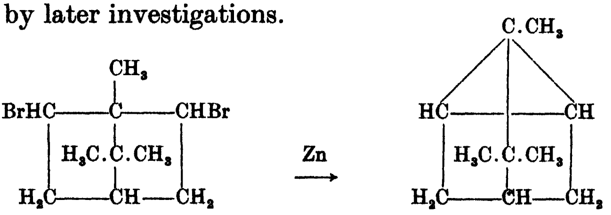
‡ Compare Nametkin and Alexandrov, *J. Russ. Phys. Chem. Soc.* 1926, **57**, 395; *ibid.* 1930, **62**, 1335.

The reduction of apobornylene to the corresponding saturated hydrocarbon does not appear to have been carried out.

TRICYCLENE (CYCLENE)



The interesting tricyclic hydrocarbon, $C_{10}H_{16}$, known as *tricyclene* or *cyclene*, was first prepared by Godlewski and Wagner[*] by the action of zinc dust on *pinene dibromide* (2:6-dibromocamphane) (I) in alcoholic solution.[†] It was shown subsequently by Wagner, Moycho and Zienkowski[‡] to be present in camphene prepared by the dehydration of *iso*borneol. It can be readily separated from the unsaturated hydrocarbon by oxidation of the latter with potassium permanganate, since it is not attacked by this reagent even on long boiling. It had been suggested by Semmler[§] that pinene dibromide was the camphane derivative (I), and in 1902[‖] he assigned to tricyclene the structure (II), which has been confirmed by later investigations.


(I) (II)

Since the pioneering investigations of Wagner and his collaborators, tricyclene has been obtained by a number of reactions, but undoubtedly the most convenient for its preparation is that devised by Meerwein and van Emster,[¶] who have shown that it

---

[*] *J. Russ. Phys. Chem. Soc.* 1896, **29**, 121.

[†] Aschan (*Ber.* 1928, **61**, 42) has shown that tricyclene is similarly formed when pinene dichloride is treated with sodium.

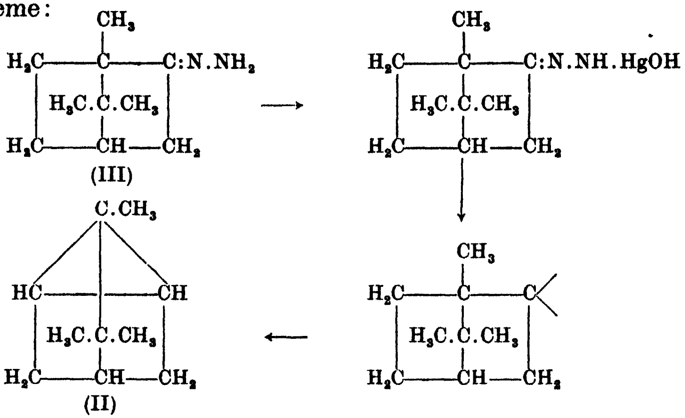
[‡] *Ber.* 1904, **37**, 1035.

[§] *Ibid.* 1900, **33**, 3423.

[‖] *Ibid.* 1902, **35**, 1019.

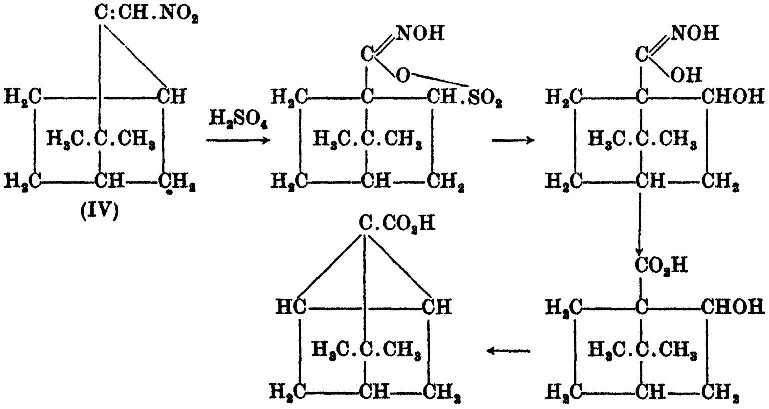
[¶] *Ibid.* 1920, **53**, 1815.

results in excellent yield when *camphorhydrazone* (III) is treated with yellow mercuric oxide in alkaline solution. They formulate the reaction as proceeding in accordance with the following scheme:


(III)

(II)

Tricyclene can be prepared also from *tricyclenic acid* (V), m.p. 151°, which Bredt and May[*] showed was formed when Jagelki's[†] "camphenilic nitrite" was treated with concentrated sulphuric acid. The mechanism of this reaction has been studied by Lipp,[‡] who, as mentioned on p. 311, has shown camphenilic nitrite to be *ω-nitrocamphene* (IV). He has suggested that the conversion into tricyclenic acid takes place in the manner outlined below.


(IV)

(V)

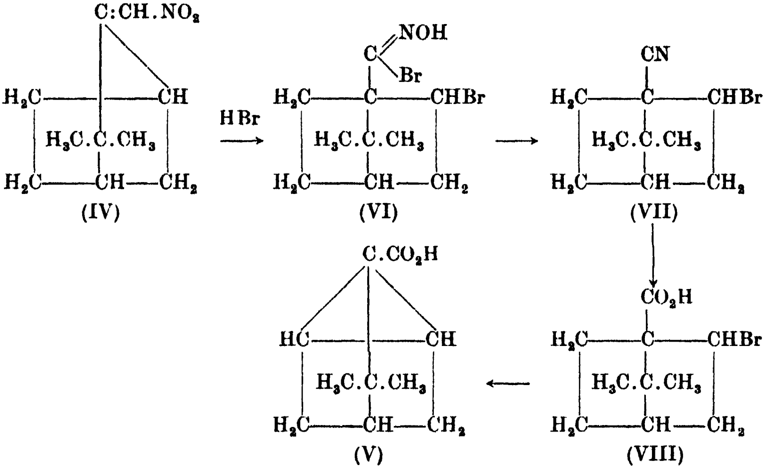
---

[*] *Chem.-Ztg.* 1909, **33**, 1265.

[†] *Ber.* 1899, **32**, 1498.

[‡] *Annalen,* 1913, **399**, 241; 1914, **402**, 343.

Although it was not found possible to separate any of the intermediate products postulated in the scheme, Lipp showed that a similar series of reactions occurred with hydrobromic acid, and in this case the intermediate *bromide* (VI) was isolated and its constitution determined by conversion into the *nitrile* (VII), m.p. 171–172°, which gave on hydrolysis the *acid* (VIII), m.p. 221–222°.



The conversion of tricyclenic acid into tricyclene has been successfully carried out by Lipp[*] and by Komppa.[†] In his first experiments Lipp reduced the *nitrile* of tricyclenic acid (IX) to the corresponding base, *ω-aminotricyclene* (X), b.p. 100–101°/27 mm., but, on attempting to convert this into the alcohol by the action of nitrous acid, molecular rearrangement occurred with the formation of *camphenilanaldehyde* (XI).

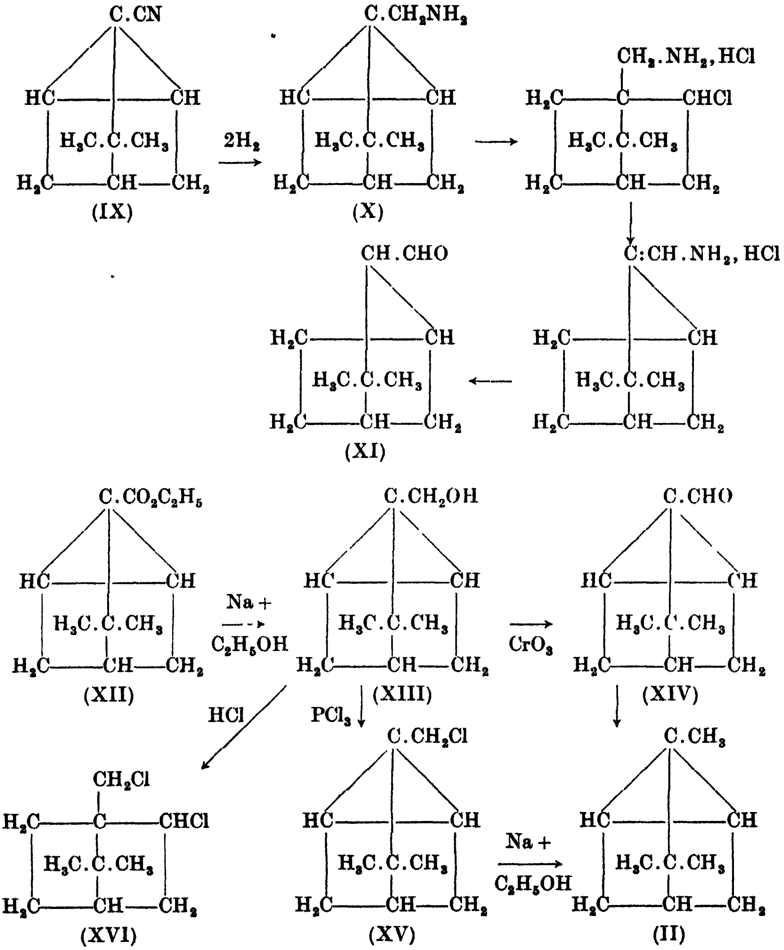
A second method was more successful. By the reduction of *ethyl tricyclenate* (XII) the alcohol, *tricyclol* (XIII), m.p. 111–112°, was obtained, which on oxidation with chromic acid gave the aldehyde, *tricyclal* (XIV), m.p. 85–90°, *semicarbazone*, m.p. 219–220°.[‡] From this, by Wolff's reaction, the hydrocarbon was prepared.

---

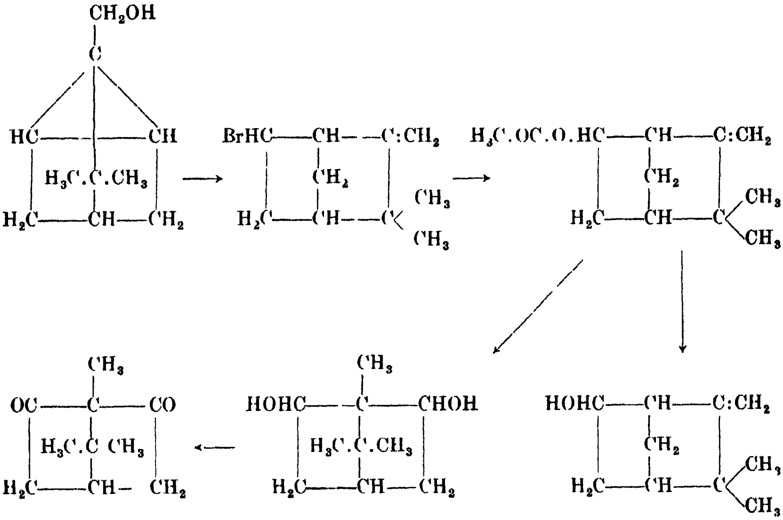
[*] *Ber.* 1920, **53**, 769.

[†] *Ibid.* 1929, **62**, 1366.

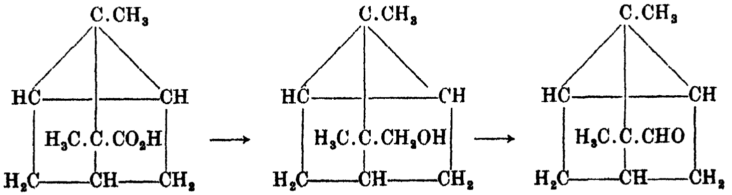
[‡] Reference has already been made (p. 312) to the formation of this aldehyde from ω-nitrocamphene; on further oxidation it gives tricyclenic acid.



Komppa adopted a somewhat similar method, but, in place of oxidising the alcohol to the aldehyde, he converted it by the action of phosphorus trichloride into the chloride, *ω-chlorotricyclene* (XV), which on reduction with sodium and alcohol gave the hydrocarbon. He also showed that treatment of the alcohol with hydrogen chloride gave 2 : 10-*dichlorocamphane* (XVI). Unlike the action of phosphorus pentachloride, rearrangement occurs when tricyclol is treated with phosphorus pentabromide, the product being 6-*bromocamphene*, which can be converted through 6-*acetoxycamphene* into 6-*hydroxycamphene*, m.p. 60°. Hydration of the 6-acetoxycamphene gives 2:6-*dihydroxycamphane*, m.p. 240–242°, which is oxidised by chromic acid to 2:6-*diketocamphane*, m.p. 192–193°. The reactions involved are shown in the scheme below:*



Of great interest is the observation of Ruzicka and Liebl† that teresantalic acid (XVII) can be converted into tricyclene. The ester of this acid on reduction gives *teresantalol*, m.p. 114°, which is oxidised by chromic acid to the *aldehyde* (XVIII), *semicarbazone*, m.p. 217°. From this semicarbazone by Wolff's reaction tricyclene was obtained.



(XVII) (XVIII)

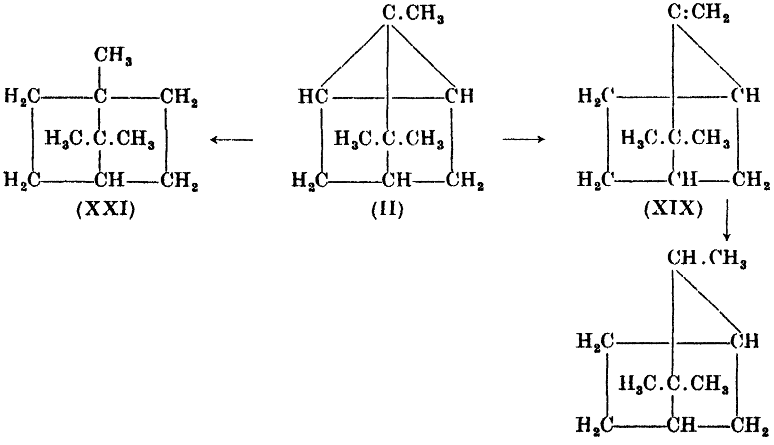
---

* Lipp, *Chem. Ber.* 1947, **80**, 165.

† *Helv. Chim. Acta*, 1926, **9**, 140.

Tricyclene, which is very volatile, melts at 67·5–68°, b.p. 153°/761 mm., $d_{4°}^{66°}$ 0·8440, $n_D^{66\cdot9°}$ 1·4405.[*] The heat of combustion has been found by Roth and Östling[†] to be practically identical with that of camphene, 1469·1 kg.-cals.

On reduction by the Sabatier-Senderens process over a nickel catalyst at 180–200°, tricyclene passes smoothly into iso*camphane* (XX), the reaction proceeding evidently with the intermediate formation of camphene (XIX), since this hydrocarbon is obtained if tricyclene is passed over the same catalyst in a current of nitrogen.[‡] According to Zelinski and Lewina[§] by passage over platinum black at 155–160° tricyclene yields *camphane* (XXI), ring fission occurring in the alternative manner.



In view of the older theories that tricyclene was an intermediate stage in the Wagner rearrangement (p. 158), the action of the halogens and the halogen acids on the hydrocarbon is of considerable interest. Meerwein and van Emster[||] prepared by the action of bromine a liquid dibromide, which was not identical with either bornyl dibromide or camphene dibromide, and they therefore consider that it is probably a true dibromotricyclene. A crystalline *chlorotricyclene* (XXIII), m.p. 134–135°, b.p. 194–195°, was obtained by Meerwein and Wortmann[¶] by the action of potassium acetate on *β-camphor dichloride* (2:4-dichlorocamphane) (XXII) in phenol solution. The chloride so obtained is not homogeneous, being mixed with *β-chlorocamphene* (XXIV), since, on reduction with sodium and alcohol, it yields a mixture of tricyclene and camphene. It is not possible to separate these two chlorides by fractional crystallisation, but on ozonolysis the chlorocamphene is oxidised, the chlorotricyclene (see p. 304) not being attacked.

---

[*] Östling, *J.C.S.* 1912, **101**, 472.

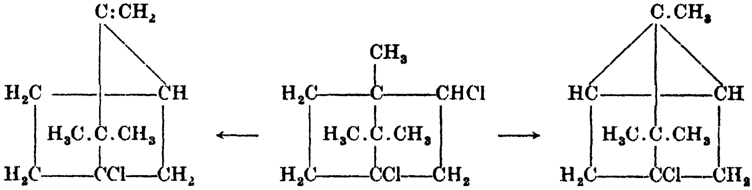
[†] *Ber.* 1913, **46**, 312.

[‡] Meerwein and van Emster, *Ber.* 1920, **53**, 1815.

[§] *Annalen*, 1929, **476**, 63.

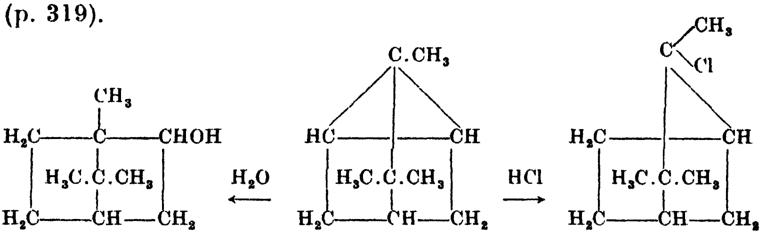
[||] *Ber.* 1920, **53**, 1815.

[¶] *Annalen*, 1924, **435**, 205.



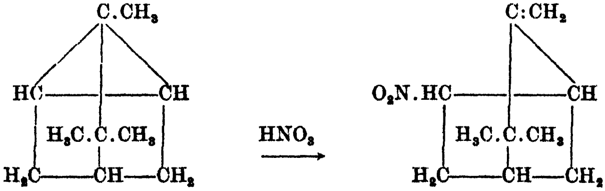
(XXIV) (XXII) (XXIII)

By the action of hydrogen chloride on an ethereal solution of tricyclene *camphene hydrochloride* (XXV) is obtained, whilst on hydration it gives a mixture of borneol and *iso*borneol (XXVI). This reaction is, however, very slow and its bearing on the mechanism of the Wagner rearrangement is discussed elsewhere (p. 319).



(XXVI) (II) (XXV)

Nametkin and Zabrodina* have shown that tricyclene, on treatment with dilute nitric acid at 125–130°, yields *α-nitrocamphene* (XXVII) (see p. 314).

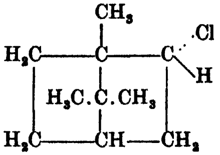


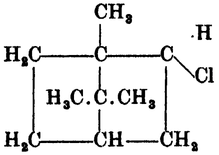
(II) (XXVII)

---

* *Annalen*, 1925, 441, 181.

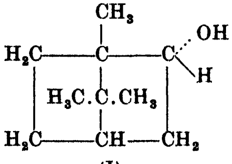
BORNYL AND ISO*BORNYL CHLORIDES*



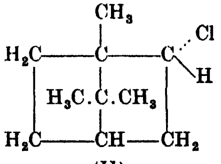


The early investigations resulting in the preparation of bornyl chloride (artificial camphor, pinene hydrochloride) have been already described on p. 106, but it is desirable to consider here the evidence upon which the constitution of this substance is based and also to discuss some of its more important reactions.

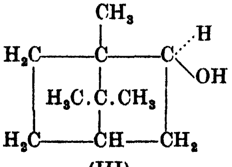
Although it was recognised by Berthelot that "artificial camphor" was not a true derivative of pinene, its constitution and the nature of its relationship to bornyl chloride and *iso*bornyl chloride (the so-called camphene hydrochloride) was not determined until much later. In 1899, Wagner and Brickner* showed "artificial camphor" to be identical with bornyl chloride (prepared from borneol), and that it was therefore a derivative of this alcohol (I), in which the hydroxyl group had been replaced by halogen. It followed therefore that it had formula (II), *iso*bornyl chloride (IV) being related in a similar manner to *iso*borneol (III).†



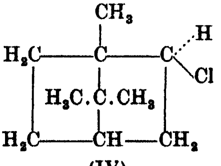
(I)



(II)



(III)



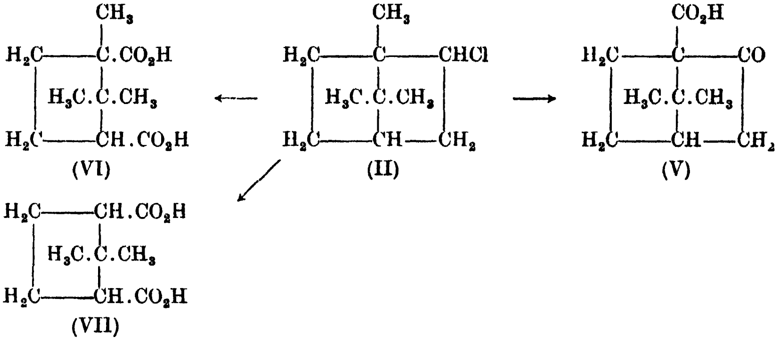
(IV)

---

* *Ber.* 1899, **32**, 2302.

† At the time the stereochemical relationship of borneol to *iso*borneol was not recognised and Wagner considered *iso*borneol to be a derivative of camphene (see p. 354).

Although bornyl chloride was very resistant to oxidising agents, direct experimental proof of the correctness of Wagner and Brickner's view was already available. In 1896, Armstrong[*] had shown that when bornyl chloride was oxidised with concentrated nitric acid at 20° *ketopinic acid* (V) (see p. 301) was obtained, whilst Garner and Cockburn[†] by the action of dilute nitric acid prepared *camphoric acid* (VI) and *apocamphoric acid* (VII), the latter acid obviously being derived from either camphene or camphene hydrochloride.


(VI) (II) (V)

(VII)

The formation of these acids by the degradation of bornyl chloride left little doubt that it contained the camphane skeleton and this was confirmed by its reduction with sodium to the saturated hydrocarbon.[‡] The position of the chlorine atom was proved by its preparation from borneol (see p. 342).

Bornyl chloride crystallises in leaflets, m.p. 132°, b.p. 207–208°. It has an odour resembling that of camphor and it is very volatile at the ordinary temperature. When prepared from optically active sources it is optically active, and it has the same sign as the hydrocarbon (or alcohol) from which it is prepared. The highest recorded rotations would appear to be the following: $[\alpha]_D$ +33·52° (in alcohol $c = 1$), $[\alpha]_D$ −33·24° (in alcohol $c = 1$).[§]

Bornyl chloride can be prepared most conveniently by treating α-pinene, dissolved in chloroform, with hydrogen chloride at 0°. Its formation has also been observed in a number of other reactions. Berthelot[*] obtained it by the action of hydrogen chloride on borneol in a sealed tube at 100°, whilst Wagner and Brickner[†] separated it in a small yield from amongst the products of the action of phosphorus pentachloride on this alcohol, the main product of the reaction being, however, *iso*bornyl chloride. Hückel and Pietrzok[‡] have shown that if a small amount of ferric chloride is added to the phosphorus pentachloride, the product is almost pure *iso*bornyl chloride. Kondakov and Schindelmeiser[§] prepared it by the action of hydrogen chloride on bornyl acetate in acetic acid solution. It may also be obtained by direct chlorination of camphane;[‖] further action yields 2:3-dichlorocamphane.[¶]

---

[*] *J.C.S.* 1896, **69**, 1397.

[†] *Ibid.* 1898, **73**, 278.

[‡] Semmler, *Ber.* 1900, **33**, 774.

[§] Thurber and Thielke, *J. Amer. C.S.* 1931, **53**, 1032.

As was mentioned above, on reduction bornyl chloride yields camphane. When treated with sodium it gives a mixture of *dibornyl*, m.p. 88–90°, camphene, and camphane;[**] the same products are also formed by the action of methyl magnesium bromide in the presence of a cobaltous chloride catalyst.[††]

Apart from its tendency to tautomerise to *iso*bornyl chloride (see below), bornyl chloride is extremely stable. Two reactions which it undergoes are of great importance and have been very thoroughly investigated. By the elimination of hydrogen chloride, as was first mentioned by Berthelot (see p. 106), it gives camphene, whilst the replacement of the halogen atom by a hydroxyl group yields *iso*borneol. Since both camphene and *iso*borneol are utilised in the manufacture of camphor, these reactions are of technical importance and have formed the subject of numerous patents. The elimination of hydrogen chloride can be effected by the action of bases, sodium hydroxide in the presence of catalysts, quinoline, higher pyridine bases, the naphthylamines, etc., whilst for the preparation of *iso*borneol or *iso*bornyl esters the salts of various fatty acids have been employed. Full references will be found in the technical literature.[‡‡]

---

[*] *Ann. Chim.* 1859 [iii], **56**, 92.

[†] *Ber.* 1899, **32**, 2302; compare Kachler, *Annalen*, 1872, **164**, 77; Wallach, *ibid.* 1885, **230**, 231.

[‡] *Annalen*, 1939, **540**, 250.

[§] *J. pr. Chem.* 1907 [ii], **75**, 533.

[‖] Gandini, *Gazzetta*, 1936, **66**, 357.

[¶] Compare Frankforter and Frary, *J. Amer. C.S.* 1906, **28**, 1464.

[**] Gandini, *Gazzetta*, 1934, **64**, 302.

[††] Kharasch, Engelmann and Urry, *J. Amer. C.S.* 1944, **66**, 365.

[‡‡] Compare *Thorpe's Dictionary of Applied Chemistry*, 4th ed. Vol. II, p. 249, London, 1938.

Interesting results have accrued from a study of the action of magnesium on bornyl chloride. This reaction was first investigated by Hesse,[*] who showed that the compound which was formed by the action of magnesium on bornyl chloride in the presence of ether was decomposed by water giving camphane, whilst, if it was subjected to the action of oxygen prior to decomposition, borneol resulted. The action of carbon dioxide on the magnesium bornyl chloride complex was very carefully studied by Houben and his collaborators.[†] The reaction proceeds normally with the formation of *camphane-2-carboxylic acid* (VIII), m.p. 78°, $[\alpha]_D$ −18·26° (in alcohol), which may be identical with the acid obtained by Bredt and Perkin[‡] by reduction of *bornylene-2-carboxylic acid.* When heated, or when warmed with acid or with alkali, it isomerises to give two new acids, needles, m.p. 85–86°, and prisms, m.p. 86–87°, both of which are still laevorotatory. The corresponding *dl*-camphane-2-carboxylic acid (from inactive bornyl chloride), m.p. 78–80°, on similar treatment gives an acid, m.p. 93–94°.[§] Under slightly different conditions the treatment of *l*-bornyl chloride with magnesium and carbon dioxide gives a *d*-camphane-2-carboxylic acid, m.p. 76–78°, which may be isomerised to a *l*-acid, m.p. 88–89°; the latter may be identical with the *acid*, m.p. 88–89° (*nitrile*, m.p. 157–158°), obtained by the action of cyanogen on bornyl magnesium chloride.[‖] In a more recent investigation, Vavon and Rivière[¶] have obtained by isomerisation of *l*-camphane-2-carboxylic acid, m.p. 77°, two acids, prisms, m.p. 82°, $[\alpha]_{5780}$ +16·3°, and leaflets, m.p. 75–76°, $[\alpha]_{5780}$ +7·4°. Furthermore, attention must be drawn to those other products which have been described as camphane-2-carboxylic acid: (i), m.p. 88–89°,[**] obtained by oxidation of *camphane-2-aldehyde*, m.p. 131°, derived by the action of formanilide on bornyl magnesium chloride;[††] (ii), m.p.

---

[*] *Ber.* 1906, **39**, 1132, 1151.

[†] Houben, *Ber.* 1905, **38**, 3799; 1906, **39**, 1701; Houben and Willfroth, *ibid.* 1913, **46**, 2283, 2530; Houben and Pfankuch, *ibid.* 1926, **59**, 956, 2285; compare Zelinski, *ibid.* 1902, **35**, 4418.

[‡] *J.C.S.* 1913, **103**, 2219.

[§] Barbier and Grignard, *Bull. Soc. chim.* 1914 [iv], **15**, 31, 36.

[‖] Grignard and Bellet, *Compt. rend.* 1912, **155**, 44.

[¶] *Compt. rend.* 1943, **216**, 251; *Bull. Soc. chim.* 1943 [v], **10**, 460; Rivière, *Ann. Chim.* 1946 [xii], **1**, 157.

[**] The optically inactive acid obtained by regeneration from the anhydride, however, had m.p. 78°.

[††] Houben and Doescher, *Ber.* 1910, **43**, 3435.

69–71°, $[\alpha]_D$ – 10°, obtained by oxidation of *camphane-2-carbinol*, m.p. 86–87°, prepared by the action of ethyl formate on bornyl magnesium chloride;[*] and (iii), m.p. 71°, $[\alpha]_D$ + 11·3°, a by-product from the action of alcoholic alkali on methyl 2-chlorocamphane-2-carboxylate (see below), and possibly identical with an acid possessing similar physical constants which was obtained by Passerini[†] by reduction of *bornylene-6-carboxylic acid*, m.p. 65–66°. Since only four active and two inactive forms are possible for the acid under discussion, some of the isomers mentioned above must either be mixtures, or structural isomerides. Vavon and Rivière consider that the existence of their products (melting at 75–76° and 82°) may be explained by steric hindrance, free rotation of the carboxyl group being restricted by the hydrogen atom on C_3, but this would appear to be highly improbable. Indeed, in view of the fact that bornyl and *iso*bornyl chlorides are tautomeric with camphene hydrochloride, it is possible that some of the acids described may be contaminated with *iso*camphane derivatives.

When camphane-2-carboxylic acid, m.p. 78°, is treated with chlorine and phosphorus pentachloride, it gives the acid chloride of 2-chlorocamphane-2-carboxylic acid (IX), m.p. 118–119°, which by the action of alkalis loses hydrogen chloride with the formation mainly of *camphene-1-carboxylic acid* (X), m.p. 109–110°. The constitution of this acid is proved by its oxidation to the *camphenilone carboxylic acid* (XI), m.p. 134°, which had been prepared previously by Aschan[‡] from camphenic acid. On reduction, it gives iso*camphane-1-carboxylic acid*, m.p. 126°.

When the acid (X) is warmed with acetic or formic acid in the presence of zinc chloride it undergoes hydration. It was originally thought that the product, m.p. 221–222°, was 6-*hydroxycamphane-2-carboxylic acid*, formed by a normal Wagner rearrangement, but it has since been formulated as 2-*hydroxycamphane-4-carboxylic acid* (XII).[§] This is produced by a change of the Nametkin type (compare p. 162) in which the intermediate hydrate (XIII) isomerises by a pinacolic rearrangement into (XIV), which then undergoes the Wagner change. Dehydration

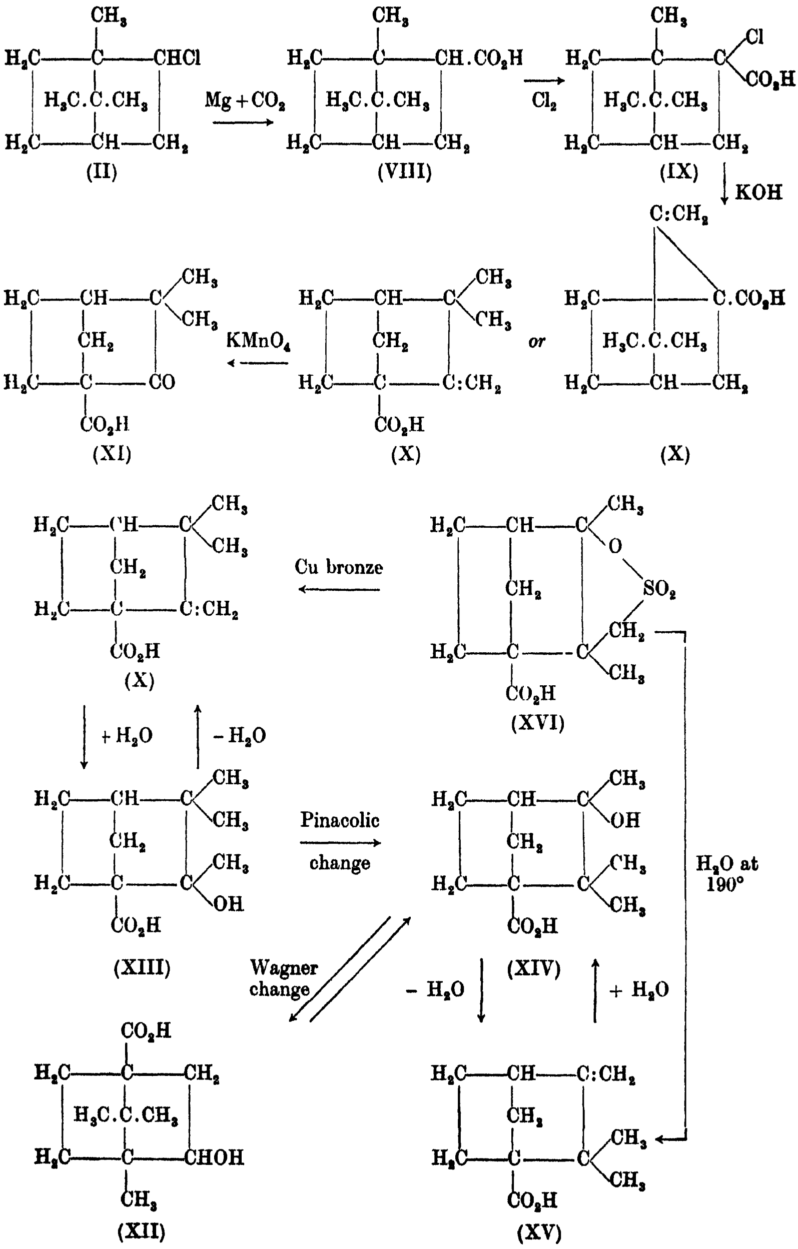
---

[*] Bousset and Vaugin, *Bull. Soc. chim.* 1930 [iv], **47**, 986.

[†] *Gazzetta*, 1924, **54**, 540.

[‡] *Annalen*, 1911, **383**, 58; 1915, **410**, 240.

[§] Houben and Pfankuch, *Annalen*, 1931, **489**, 193.


(II) (VIII) (IX) (X) (XI) (X) (X) (X) (XVI) (XIII) (XIV) (XII) (XV)

of the hydroxy-acid (XIV) gives l-*camphene*-4-*carboxylic acid* (XV), m.p. 159–160° (*dl*-form, m.p. 131°), which regenerates the same hydroxy-acid on hydration, and on reduction yields iso-*camphane*-4-*carboxylic acid*, m.p. 170°. A precisely similar series of reactions can be brought about by the treatment of camphene-1-carboxylic acid with hydrogen chloride;[*] 2-*chlorocamphane*-4-*carboxylic acid*, m.p. 164–165°, is thereby obtained, and it is also formed under similar conditions from camphene-4-carboxylic acid, into which it is converted by elimination of hydrogen chloride. Sulphuric acid, also, may be used, an intermediate product then being *camphenehydrato*-4-*carboxylo*-π-*sulpholactone* (XVI); Asahina and Kawahata have shown that this substance gives camphene-1-carboxylic acid on treatment with copper bronze, whilst when heated under pressure with water at 190° it gives the isomeric 4-carboxylic acid.

iso*Bornyl chloride*, which was formerly known as camphene hydrochloride, was first prepared by Berthelot[†] by the action of hydrogen chloride on camphene in alcoholic solution. He showed further that it could readily be reconverted into camphene. The formation of this hydrochloride, m.p. 147°, from camphene was confirmed by Riban,[‡] who observed that *l*-camphene ($[\alpha]_D$ −51·04°) gave *d*-*iso*bornyl chloride, $[\alpha]_D$ +30·25°, from which, by the elimination of hydrogen chloride, *l*-camphene, $[\alpha]_D$ −8·5°, was obtained. The same chloride was prepared by Kachler[§] by the action of phosphorus pentachloride on borneol, whilst Jünger and Klages[‖] and Reychler[¶] described its preparation by the action of this reagent on *iso*borneol. The identity of the chloride prepared by these various methods was not however fully recognised, and this, together with the problem of the relationship of bornyl and *iso*bornyl chlorides, gave rise to a considerable controversy, into which it is unnecessary to enter here. There can be no doubt that these two chlorides are related to one another in exactly the same manner as borneol and *iso*borneol, being *cis*-*trans*-isomerides, although this view does not appear to be shared by Aschan.[**] Final proof that *iso*bornyl chloride was not camphene hydrochloride was provided by the preparation of this substance by Aschan (see p. 307). On reduction with sodium, *iso*bornyl chloride, like bornyl chloride, yields camphane,* and in its general chemical behaviour it resembles this chloride, although there are considerable differences in the facility with which the reactions proceed. Differences of exactly the same kind are observed in the case of borneol and *iso*borneol and are doubtless due to their spatial configurations. *iso*Bornyl chloride is much less stable than bornyl chloride and, on boiling with water, elimination of hydrogen chloride with formation of camphene occurs. This hydrocarbon is also obtained by the action of alkalis; in this connection, it is, however, of particular interest to note that by the action of milk of lime at 50–60° Aschan[†] obtained camphene hydrate (see p. 317). When *iso*bornyl chloride is heated with acetic acid it yields *iso*bornyl acetate.

---

[*] Asahina and Kawahata, *Ber.* 1939, **72**, 1540.

[†] *Annalen*, 1859, **110**, 367; *Compt. rend.* 1862, **55**, 497.

[‡] *Ann. Chim.* 1875 [v], **6**, 363.

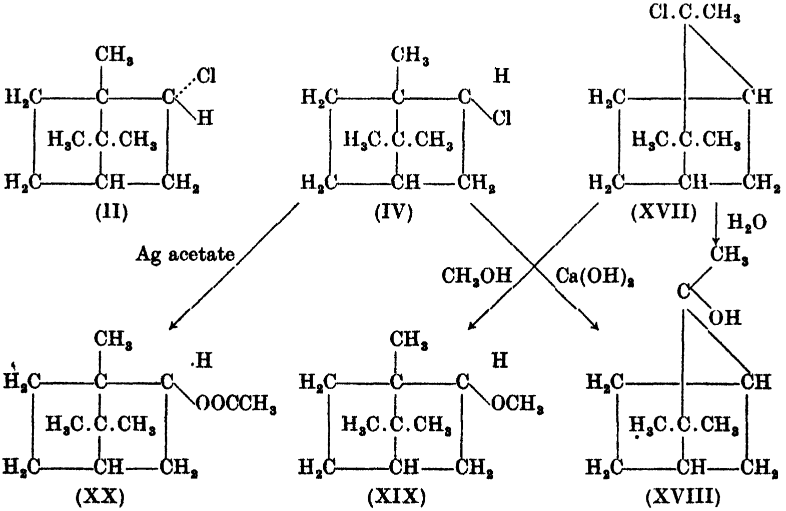
[§] *Annalen*, 1879, **197**, 93.

[‖] *Ber.* 1896, **29**, 544.

[¶] *Ibid.* p. 697.

[**] *Naphtenverbindungen, Terpene und Campherarten*, p. 180.

The relationship of bornyl chloride (II), *iso*bornyl chloride (IV) and camphene hydrochloride (XVII) to one another has formed the subject of two important papers by Meerwein and van Emster,[‡] to which reference has already been made. By a series of well-conceived kinetic experiments, they have shown



---

[*] Semmler, *Ber.* 1900, **33**, 3429.

[†] *Ber.* 1908, **41**, 1092.

[‡] *Ibid.* 1920, **53**, 1821; 1922, **55**, 2506.

that these three chlorides are true tautomerides. As typical examples illustrating the tautomerism of *iso*bornyl chloride and camphene hydrochloride the following may be quoted: (i) camphene hydrochloride (XVII) gives with water camphene hydrate (XVIII), whilst by the action of methyl alcohol *iso*bornyl methyl ether (XIX) is obtained; (ii) *iso*bornyl chloride (IV) gives with silver acetate *iso*bornyl acetate (XX), with milk of lime camphene hydrate (XVIII).

The rate of conversion of camphene hydrochloride into *iso*bornyl chloride can be followed quantitatively by taking advantage of the property referred to already on p. 308, that the former titrates in solution like free hydrochloric acid. As has been observed in other cases of tautomerism, the velocity of the change is dependent upon the nature of the solvent, and this effect is very noticeable in the reaction camphene hydrochloride → *iso*bornyl chloride. In ethereal solution, camphene hydrochloride is remarkably stable, whilst in nitromethane at 20° 50 per cent. is converted into *iso*bornyl chloride in 1½ hr. The reaction velocity is related directly to the dielectric constant of the solvent, increasing as this increases. A marked influence is exerted also by catalysts, the velocity being enormously increased by the addition of stannous chloride, hydrogen chloride, phenols, etc.[*] As is the case with any true tautomeric change, the reaction is never complete and is reversible. It appears probable that the initial stage is a rate-controlling ionisation of the chlorine atom; the "camphene hydro-" cation so produced tautomerises to the bornyl cation, which, with Walden inversion, recaptures a chloride ion and forms *iso*bornyl chloride.[†] The ionic nature of this and similar reactions is probably the cause of the racemisation, either partial or complete, which occurs in reactions such as *l*-camphene → *d*-*iso*bornyl chloride → *l*-camphene.[‡]

A similar tautomerism exists also between bornyl chloride and *iso*bornyl chloride, but in this case the change is more difficult to follow. Meerwein and van Emster observed, however, that if *iso*bornyl chloride is dissolved in chlorobenzene containing some stannous chloride and the solution maintained at 100° for 20 hr., an equilibrium mixture was obtained containing approximately *iso*bornyl chloride 15·1 per cent., camphene hydrochloride 3·8 per cent. and bornyl chloride 74·1 per cent.

---

[*] Compare Bartlett and Pöckel, *J. Amer. C.S.* 1938, **60**, 1585; Bartlett and Gill, *ibid.* 1941, **63**, 1273.

[†] Compare Bateman, Cooper, Hughes and Ingold, *J.C.S.* 1940, p. 930; Nevell, de Salas and Wilson, *J.C.S.* 1939, p. 1188.

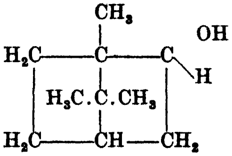
[‡] Meerwein and Monfort, *Annalen*, 1923, **435**, 207. See also p. 304.

In view of its tautomeric nature, it is not surprising that the melting-point recorded for *iso*bornyl chloride shows very marked variations (from 146 to 165°). Meerwein and van Emster state that the pure chloride melts at 161·5°. The more important reactions of the chloride have been discussed already.

Corresponding to bornyl chloride and *iso*bornyl chloride, the bromides and iodides have been prepared. *Bornyl bromide* melts at 92° and resembles bornyl chloride very closely in its properties,[*] whilst iso*bornyl* bromide melts at 133°.[†] According to Aschan,[‡] *bornyl iodide* is best prepared by the addition of bornyl chloride to an ethereal solution of magnesium iodide. It melts at -3 to $-5°$, b.p. 99–100°/6 mm., $d_{4^\circ}^{20^\circ}$ 1·4553, $[\alpha]_D$ $+16{\cdot}02°$. The preparation of *iso*bornyl iodides has been described by Wagner and Brickner[§] and by other investigators, but the homogeneity of the iodide would appear doubtful.

B. ALCOHOLS

BORNEOL



The secondary alcohol, borneol, $C_{10}H_{18}O$, occurs somewhat widely distributed in nature both in the free state and in the form of its esters. *d*-Borneol, "Borneocamphor", forms the main constituent of the oil from *Dryobalanops aromatica* Gaertn., whilst *l*-borneol, "Ngai-camphor", occurs in that obtained from *Blumea balsamifera*. *dl*-Borneol is also found in a number of other oils.[||]

---

[*] Wallach, *Annalen*, 1887, **239**, 7.

[†] Semmler, *Ber.* 1900, **33**, 3428.

[‡] *Ber.* 1912, **45**, 2395.

[§] *Ibid.* 1899, **32**, 2320.

[||] Compare Gildemeister and Hoffmann, *Die Ätherischen Öle*, 3rd ed. I, 475.

Owing to its being a crystalline solid, borneol is one of the constituents of essential oils which has been longest known, but in the early literature it is not infrequently confused with camphor. The first scientific investigation was due apparently to Pelouze,[*] who examined the oil of *Dryobalanops aromatica* and showed the "camphor" which it contained to have the composition $C_{10}H_{18}O$, melting at 198° and boiling at 212°. Biot[†] observed that it was dextrorotatory in alcoholic solution. By the action of phosphorus pentoxide Pelouze obtained a hydrocarbon, $C_{10}H_{16}$, and by oxidation a substance which had all the properties of the camphor derived from *Cinnamonum Camphora*. Simultaneously, the "camphor" prepared from oil of valerian (*Valeriana officinalis* L.) was under investigation,[‡] and was considered by Gerhardt to be identical with borneocamphor. He introduced the name borneol, and he made the important suggestion that camphor and borneol were related to one another as aldehyde and alcohol. Proof that borneol was an alcohol was first supplied by the work of Berthelot,[§] who prepared bornyl esters by its interaction with stearic and benzoic acids. At the same time Berthelot found that borneol could be prepared from camphor by the action of an alcoholic solution of potassium hydroxide, when, in addition to borneol, a second alcohol of the same composition, but with a different rotatory power, was formed. For the synthetic borneol Berthelot introduced the name "camphol" and in collaboration with Buignet[‖] he described another "camphol", which they prepared by the action of alkali on amber resin. This differed from borneocamphor and camphol in having a very low rotatory power. Berthelot observed further that camphol gave on treatment with hydrogen chloride a hydrochloride resembling closely in its properties "artificial camphor". A more convenient method for the reduction of camphor to borneol was devised by Baubigny,[¶] who treated the ketone with sodium in toluene solution. After solution of the sodium, the mixture was saturated with carbon dioxide and water added, when borneol separated, the camphorcarboxylic acid, which was formed simultaneously, remaining in solution. Baubigny observed, however, that the *d*-borneol prepared in this manner was not homogeneous, a second alcohol, which was laevorotatory, being also formed. A more detailed study of these two reactions was made by Kachler.[*] He concluded that Baubigny's reaction proceeded in the following stages:

---

[*] *Compt. rend.* 1840, **11**, 365; *Annalen*, 1841, **40**, 326.

[†] *Compt. rend.* 1840, **11**, 374.

[‡] Gerhardt and Cahours, *Annalen*, 1841, **38**, 69; Gerhardt, *ibid.* 1843, **45**, 29.

[§] *Ann. Chim.* 1859 [iii], **16**, 51.

[‖] *Compt. rend.* 1860, **50**, 606; *Annalen*, 1860, **115**, 244.

Ann. Chim. 1870 [iv], **19**, 221.

$$\begin{array}{llllll}
\underset{\text{(camphor)}}{2C_{10}H_{16}O} & + 2Na & \longrightarrow & \underset{\text{(sodium deriv. of camphor)}}{C_{10}H_{15}ONa} & + & \underset{\text{(sodium deriv. of borneol)}}{C_{10}H_{17}ONa} \\
C_{10}H_{17}ONa & + CO_2 & \longrightarrow & C_{10}H_{17}ONa, CO_2 & & \\
C_{10}H_{17}ONaCO_2 & + H_2O & \longrightarrow & C_{10}H_{17}OH & + & NaHCO_3
\end{array}$$

Borneol was thus a saturated secondary alcohol and camphor the corresponding ketone. He prepared by the action of hydrogen chloride and phosphorus pentachloride a chloride, m.p. 157°, and by the action of phosphorus pentoxide a hydrocarbon, "borneene". Some years later Kachler and Spitzer[†] showed that this chloride when treated with alkalis gave camphene, whilst by the action of silver acetate bornyl acetate was obtained. The action of sodium on both *d*- and *l*-camphors was studied by Montgolfier.[‡] He succeeded in preparing from *d*-camphor a dextrorotatory and laevorotatory alcohol and from *l*-camphor a laevorotatory and dextrorotatory alcohol. The laevorotatory alcohol from *d*-camphor and the dextrorotatory alcohol from *l*-camphor were not stable and the former was converted, either by the action of heat or by warming with organic acids (stearic, acetic, benzoic acids), into the stable dextrorotatory alcohol. This stable alcohol, *camphol stable*, was identical with natural borneocamphor. The two less stable alcohols were designated *camphols instables* and are now known to be the *d*- and *l*-modifications of *iso*borneol.

Since the formation of borneol and *iso*borneol by the action of sodium on camphor is accompanied by that of camphor carboxylic acid, the yield is poor and a great advance was made by the discovery of Jackson and Menke[§] that camphor could be reduced to borneol by sodium in alcoholic solution. Although this method of preparation was criticised by Kachler and Spitzer,[*] who stated that the borneol prepared by this method was always contaminated with camphor, the later experiments of Immendorf,[†] Jackson[‡] and Wallach[§] fully substantiated the original claims of Jackson and Menke.

---

[*] *Annalen*, 1872, **162**, 259; 1873, **169**, 168.
[†] *Ibid.* 1879, **197**, 86; **200**, 340.
[‡] *Compt. rend.* 1876, **83**, 341; 1879, **89**, 101.
[§] *Amer. Chem. J.* 1884, **5**, 270.

Before proceeding to consider the experiments of Haller on the relationship of borneol and *iso*borneol to one another, reference must be made to the fundamental observation of Bouchardat and Lafont,[‖] who found that when oil of turpentine was heated at 100° with acetic acid an optically inactive borneol, m.p. 185·5–190°, was obtained. These authors then proceeded to investigate in great detail the conditions governing the hydration of pinene and they showed[¶] that both the optically active modifications of borneol and *iso*borneol could be prepared, their sign depending upon that of the hydrocarbon used in their preparation.

Three methods were available therefore for the preparation of borneol and *iso*borneol: (i) the reduction of camphor by sodium in a neutral solvent, (ii) the reduction of camphor by sodium in alcoholic solution, and (iii) the hydration of pinene and camphene. Although it was known that Montgolfier's *camphols stables* and *instables* both gave camphor on oxidation, the structural relationship of the two alcohols was not at all clear and the properties of *iso*borneol had not been studied in any detail. The elaborate investigations of Haller, which extended over some six years, and which are summarised in his memoir published in 1892,[**] did much to clarify the position and to provide a firm experimental basis for future investigations. Dealing in the first place with the natural alcohols, Haller was able to show that *d*-borneol, m.p. 208·5°, $[\alpha]_D$ + 37·33°, from *Dryobalanops aromatica*, was the optical enantiomorph of *l*-borneol from *Blumea balsamifera*, the former giving on oxidation *d*-camphor and the latter *l*-camphor. Berthelot's "camphol" from amber was a mixture of the two. In order to investigate Montgolfier's stable and unstable alcohols,

---

[*] *Monatsh.* 1884, **5**, 50.

[†] *Ber.* 1884, **17**, 1036.

[‡] *Amer. Chem. J.* 1884, **6**, 404.

[§] *Annalen*, 1885, **230**, 223.

[‖] *Compt. rend.* 1886, **102**, 171; 1887, **105**, 1177.

[¶] *Ibid.* 1887, **104**, 1717; *Bull. Soc. chim.* 1887 [ii], **48**, 781; *Ann. Chim.* 1887 [vi], **9**, 509; 1888 [vi], **15**, 145; 1889 [vi], **16**, 236.

[**] *Ann. Chim.* 1892 [vi], **27**, 392.

Haller devised a method for the separation of these in a state of purity. Direct separation of the two by fractional crystallisation was not possible, and Montgolfier had obtained the "stable" alcohol by treatment of the mixture with stearic acid at 275°, when the stearate of this alcohol was formed, the unstable alcohol being converted into camphene. Haller found that, if the acetate of the mixture of alcohols was prepared the "stable" alcohol gave a crystalline acetate, that of the unstable alcohol being an oil. By the hydrolysis of these two acetates the corresponding alcohols could be obtained.

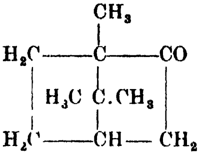
The "stable" alcohol, α-camphol, was, when prepared from *d*-camphor, identical in all respects with natural *d*-borneol from *Dryobalanops aromatica*, that derived from *l*-camphor being similarly identical with *l*-borneol. The unstable alcohol, β-camphol, *iso*camphol or *iso*borneol, was considered by Haller to be a stereoisomeride of borneol. *d*-Camphor gave *l*-*iso*borneol, m.p. 212°, $[\alpha]_D - 33{\cdot}11°$, whilst *l*-camphor gave the optical enantiomorph, *d*-*iso*borneol. Borneol and *iso*borneol had very similar properties; the latter alcohol was the more soluble and, although both alcohols gave on dehydration camphene, the elimination of water from *iso*borneol took place much more readily.

The view that borneol and *iso*borneol had the same structure and that they were stereoisomerides was generally held at this time and was supported apparently by the fact that, although the percentage composition of the mixture might vary, any reaction which led to the formation of the one alcohol always gave the other. Thus Bertram and Walbaum* found that *iso*borneol could be prepared very conveniently by the hydration of camphene with sulphuric-acetic acid mixture, little bornyl acetate being obtained, and Beckmann† showed that the percentage composition of the mixture of borneol and *iso*borneol, resulting from the reduction of camphor with sodium in neutral or in alcoholic solution, was dependent upon the temperature of the reaction and the quantity of sodium employed. Since the two alcohols were apparently the secondary alcohols corresponding to camphor, it followed, adopting Bredt's formula (I) for the latter, that they must be the stereoisomerides represented by (II) and (III).

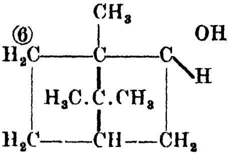
---

* *J. pr. Chem.* 1894 [ii], **49**, 1.

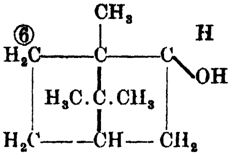
† *Ibid.* 1897 [ii], **55**, 31.



(I)

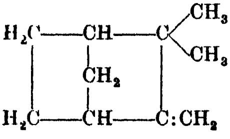


(II)

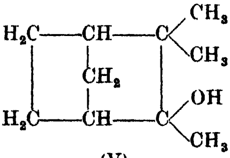


(III)

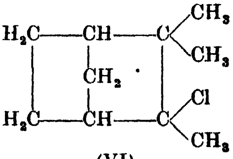
The first suggestion that borneol and *iso*borneol were structural and not stereoisomerides would appear to have been due to Wagner.* For the reasons which have been given on p. 284 he had advanced for camphene the formula represented by (IV), and since *iso*borneol was not only very readily prepared from this hydrocarbon, but could also be very readily dehydrated to it, he suggested that it was the tertiary alcohol (V), a molecular rearrangement having occurred in the reduction of camphor.



(IV)



(V)



(VI)

The following considerations appeared to support this conclusion. Semmler† found that *iso*borneol on treatment with zinc dust behaved like a tertiary alcohol, yielding a saturated hydrocarbon, $C_{10}H_{18}$, identical with *iso*camphane. The so-called camphene hydrochloride, actually *iso*bornyl chloride, could be prepared by the action of hydrogen chloride on either camphene or *iso*borneol. Subsequent investigations have, however, shown the conclusions drawn from these experiments to be incorrect. Much of the evidence has already been discussed in detail, so that only very brief reference to it will be necessary here.

Lipp‡ had pointed out that Semmler's reduction of *iso*borneol to *iso*camphane need not be regarded as a direct reduction of an alcohol to a saturated hydrocarbon, since it was not improbably preceded by a preliminary dehydration to camphene which was then reduced. This interpretation of Semmler's experiment he confirmed,[*] and showed that if the zinc dust be perfectly dry only camphene and no *iso*camphane is produced, a similar change being brought about by other dehydrating agents such as silica-gel, alumina or animal charcoal. Further, two isomeric tertiary alcohols, camphene hydrate and methyl camphenilol, which undoubtedly have structure (V), have been prepared, the former by Aschan by the action of milk of lime on bornyl chloride (see p. 317), and the latter by Moycho and Zienkowski by the action of methyl magnesium iodide on camphenilone (p. 289). The true camphene hydrochloride (VI) has been described by Aschan (p. 307) and has been shown by Meerwein and van Emster to be tautomeric with bornyl and *iso*bornyl chlorides (p. 347). Kenyon and Priston[†] pointed out that *iso*borneol must be a secondary alcohol, since it reacts readily with phthalic anhydride to give a hydrogen phthalate, a reaction which is known not to occur with tertiary alcohols. Finally, attention may be directed to the important observations of Meerwein and his collaborators, who have shown very conclusively that borneol, *iso*borneol and camphene hydrate are, like the corresponding chlorides, true tautomerides (p. 347). It would therefore appear to be rigidly established that borneol and *iso*borneol are stereoisomerides and that they must be the two secondary alcohols represented by (II) and (III), although there has been considerable controversy over the precise allocation of configurations. The ready dehydration to camphene, which is shown by *iso*borneol, was once thought[‡] to indicate for this isomer the *endo*-structure (II), in which the hydroxyl group, being on the opposite side of the *cyclo*hexane ring to the bridge, is in closer proximity to the hydrogen atom on C_6 than is the case for the *exo*-structure (III). This view, which was contrary to the conclusions reached by Vavon and Peignier[§] from a determination of the rates of hydrolysis and formation of the esters of borneol and *iso*borneol, has been rendered inconclusive by the recognition of the frequent occurrence of *trans*-elimination in such dehydrations,[‖] but has nevertheless been supported by Alder and Stein[*] from the results of their experiments on the stereochemistry of products formed by the diene reaction. These authors have shown that the ester of endo-*norcamphane-2-carboxylic acid* (VII) on treatment with sodium methoxide gives the ester of the *exo*-acid (VIII); from these acids, by the Hofmann and Curtius degradations, the corresponding norbornylamines (IX) and (X) are formed,[†] both of which, on treatment with nitrous acid, give the same alcohol, *β-norborneol.* This is assumed to be the *exo*-compound (XI) by analogy with the change of the *endo*-acid (VII) into the more stable *exo*-form (VIII). The stereoisomeric *endo*-alcohol, *α-norborneol* (XII), is obtained by the catalytic reduction of norcamphor,[‡] and since this is much less resistant to dehydration than *β*-norborneol, it is concluded that *α*-norborneol is configurationally related to *iso*borneol, and *β*-norborneol to borneol.[§]

---

* *J. Russ. Phys. Chem. Soc.* 1899, **31**, 680.

† *Ber.* 1900, **33**, 774.

‡ *Annalen*, 1911, **382**, 268.

---

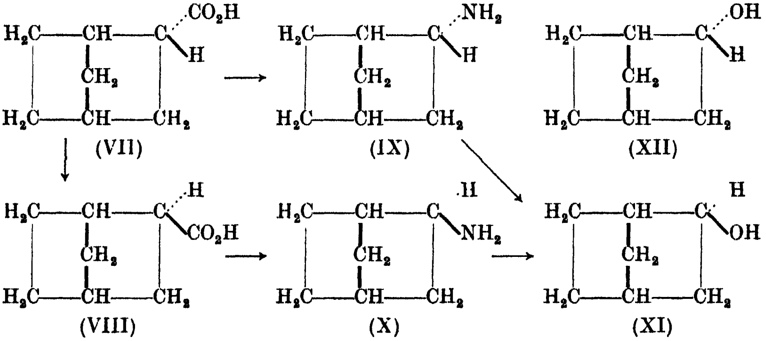
[*] *Annalen*, 1930, **480**, 298.

[†] *J.C.S.* 1925, **127**, 1472.

[‡] Lipp, *Annalen*, 1930, **480**, 298.

[§] *Bull. Soc. chim.* 1924 [iv], **35**, 925; 1926 [iv], **39**, 924.

[‖] Compare the stereochemistry of the menthols, Vol. I, p. 238.



This assignment of an *endo*-structure to *iso*borneol is also advocated by Bode[‖] on the basis of molecular refraction measurements, but other physico-chemical evidence appears to point in the other direction; Komppa and Nyman[¶] for example, from the degree of association in benzene solution, take the opposite view, which is also shared by Hückel.* Furthermore, the Vavon and Peignier suggestion is strongly supported by evidence of a purely chemical nature which has been provided by Asahina and Sano.† Reduction of ketodihydroteresantalic acid (*iso*ketopinic acid) (XIII) with sodium and alcohol gave mainly the *endo*-hydroxy-acid, d-cis-*π-apoborneol-7-carboxylic acid* (XIV), m.p. 278°, which was readily separated from the *exo*-isomer, since the latter was present in the form of its *lactone* (XV), m.p. 191° (see p. 269). The hydroxy-acid (XIV) was then acetylated, and converted by the Rosenmund procedure through the acid chloride into the aldehyde (XVI), the semicarbazone of which, on reduction with sodium ethoxide under the Kishner-Wolff conditions, gave *d*-borneol, which must therefore have the *endo*-structure (II).‡ A more recent chemical proof by Toivonen, which leads to the same conclusion, is referred to on p. 362.

---

[*] *Annalen,* 1934, **514**, 211; 1936, **525**, 183.

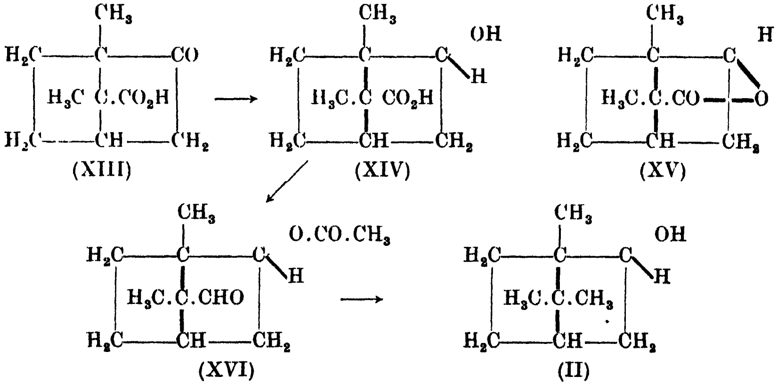
[†] Komppa and Beckmann, *ibid.* 1934, **512**, 172.

[‡] This fact, in the light of the known mode of addition of hydrogen in the catalytic reduction of the *bicyclo*heptane system, also supports the *endo*-configuration for α-norborneol.

[§] It should be noted, however, that whereas *iso*borneol on dehydration yields camphene, α-norborneol gives *norbornylene.*

[‖] *Ber.* 1937, **70**, 1167.

[¶] *Ibid.* 1936, **69**, 334.


(XIII) (XIV) (XV) (XVI) (II)

In the opinion of the writers, it is doubtful whether all the assumptions made by Alder and Stein are justified, and the balance of evidence certainly favours the assignment of the *endo*-structure (II) to borneol.

A synthesis of borneol has been described by Alder and Windemuth.§ The condensation of 1:5:5-trimethyl-$\Delta^{1:3}$-*cyclo*-

---

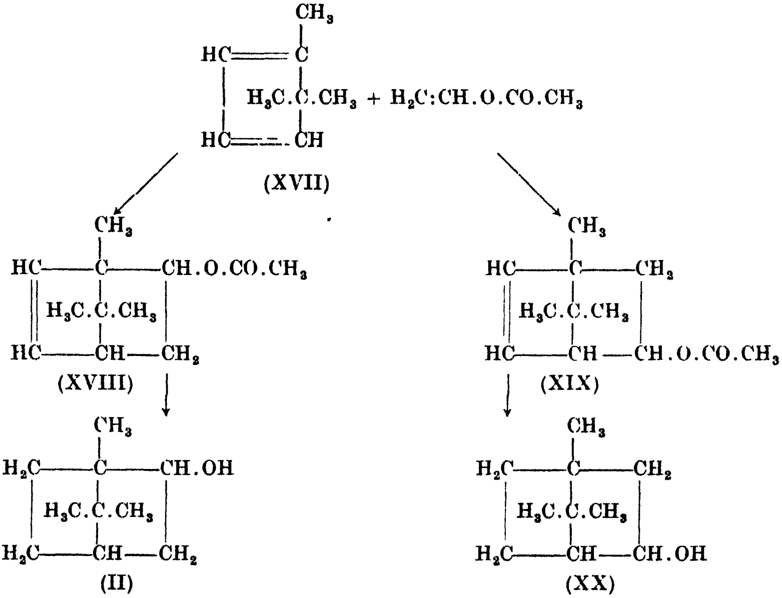
* *Annalen*, 1930, **477**, 157; *Die Chemie*, 1942, **55**, 227.

† *Ber.* 1936, **69**, 343; compare Asahina and Ishidate, *ibid.* 1935, **68**, 555.

‡ A control experiment showed that *iso*borneol would not be isomerised to borneol under the conditions employed.

§ *Annalen*, 1939, **543**, 41.

pentadiene (XVII) with vinyl acetate gives a mixture of *dehydrobornyl* (XVIII) and *dehydroepibornyl* (XIX) *acetates*, which on reduction and saponification yields *dl*-borneol, m.p. 204° (II), and *dl*-epiborneol (XX), m.p. 175–176°, which are separated by fractional crystallisation of their 3:5-*dinitrobenzoates*, m.p. 154–155° and 105° respectively.



The complete rational synthesis of borneol follows also from that of camphoric acid and camphor (p. 382). According to Achmatowicz[*] an isomeric borneol, *endoborneol*, m.p. 186°, b.p. 203–204°, *phenylurethane*, m.p. 138–139°, is obtained when bornyl acetate, prepared by the acetylation of borneol in the presence of either sulphuric acid or zinc chloride, is hydrolysed (compare p. 329). Its relationship to borneol and *iso*borneol has not been determined; it is most unlikely to be a new stereoisomer, since apart from *iso*borneol no other stable stereoisomer of borneol would be expected to exist. It must be mentioned, however, that this difficulty was avoided by Krestinski[†] by the assertion that whilst endoborneol is a true stereoisomer of borneol, *iso*borneol,

[*] *Rocz. chem.* 1926, 6, 804.

[†] *J. Gen. Chem. Russ.* 1937, 7, 415, 423.

as originally postulated by Wagner and by Semmler, is a structurally isomeric tertiary alcohol, formulated as 1-hydroxy*iso*camphane. For the reasons mentioned on p. 355 this supposition cannot be accepted and it has also been disproved by Lipp and Knapp,[*] who have prepared 1-hydroxy*iso*camphane, and shown it to possess properties quite different from those of *iso*borneol.

Borneol can be most readily identified and distinguished from *iso*borneol by the preparation of the p-*nitrobenzoate*, m.p. 137°.[†] Aschan[‡] has devised a method for distinguishing between borneol, *iso*borneol and camphene hydrate. The alcohols are dissolved in acetic acid and after the addition of sulphuric acid (50 per cent.) the solution is boiled for a few seconds. On cooling the solution containing borneol, the alcohol crystallises unchanged, the *iso*borneol solution becomes milky at 10°, but clarifies at 18–20°, whilst that containing camphene hydrate gives two layers owing to its rapid dehydration to camphene.

Borneol crystallises in the hexagonal system and has an odour resembling that of camphor, although somewhat sharper. The *d*- and *l*-forms melt at 208·5°, b p. 212°, the *dl*- has m.p. 210·3°. The optical rotatory power of the two alcohols in toluene solution was determined by Pickard and Littlebury[§] who, in agreement with Haller,[‖] found it to be $[\alpha]_D \pm 37{\cdot}92°$ ($c = 11{\cdot}5$). The rotatory dispersion of borneol and of a large number of its esters has been studied with great care by Pickard and his collaborators.[¶] According to Hantzsch,[**] borneol shows a very weak absorption in the ultra-violet region of the spectrum.

The most convenient methods for the preparation of borneol have been referred to already. It is obtained mixed with *iso*borneol when bornyl magnesium chloride is oxidised either with dry air or oxygen.[††] According to Vavon and Berton,[‡‡] approximately equal quantities of borneol and *iso*borneol are formed in this reaction, very little racemisation occurring. If the temperature is allowed to rise during the oxidation, the yield of *iso*borneol is diminished. Borneol can be obtained also by the electrolytic reduction of camphor.[*] For the purification of the alcohol and for its separation from *iso*borneol various methods have been used. Pickard and Littlebury[†] removed the *iso*borneol by digestion of the mixture with zinc chloride in benzene solution, when this alcohol was dehydrated to camphene, and the borneol was then purified through its crystalline hydrogen phthalate. If no solvent and a high temperature are used, then borneol is also attacked by the zinc chloride yielding a mixture of an ether, $(C_{10}H_{17})_2O$, m.p. 43–44°, and a *diterpene*, $C_{20}H_{32}$, b.p. 168–169°.[‡] Clark and Read[§] have applied the method which was successful in the menthol series.[||] The crude *d*-borneol is converted into its sodium derivative and condensed with chloroacetic acid to give a crude *d*-bornoxyacetic acid, from which, via the acid chloride, d-*bornyl* d-*bornoxyacetate*, m.p. 72°, $[\alpha]_D^{20}$ +63·3° (in chloroform) is prepared after purification by crystallisation. On saponification this gives pure *d*-borneol and pure d-*bornoxyacetic acid*, m.p. 76°, $[\alpha]_D^{20°}$ +59·1° (in alcohol);[¶] the acid may then be used again. This procedure could also be applied to the resolution of large quantities of *dl*-borneol.

---

[*] *Ber.* 1940, **73**, 915.

[†] Henderson and Heilbron, *Proc. C.S.* 1913, **29**, 381.

[‡] *Annalen*, 1915, **410**, 230.

[§] *J.C.S.* 1907, **91**, 1973.

[‖] *Ann. Chim.* 1892 [vi], **27**, 424.

[¶] *J.C.S* 1915, **107**, 35; 1925, **127**, 1472; compare Darmois, *Ann. Chim.* 1911 [viii], **22**, 546; Minguin, *ibid.* 1915 [ix], **3**, 368; Tschugaev, *Bull. Soc. chim.* 1913 [iv], **13**, 793; McAlpine, *J.C.S.* 1932, pp 543, 912; Huckel and Kaluba, *Annalen*, 1942, **550**, 269.

[**] *Ber.* 1912, **45**, 553.

[††] Hesse, *Ber.* 1906, **39**, 1128; Houben, *ibid.* p. 1701; Barbier and Grignard, *Bull. Soc. chim.* 1910 [iv], **7**, 344.

[‡‡] *Bull. Soc. chim.* 1925 [iv], **33**, 218.

d-Borneol is not attacked by any of the ordinary reducing agents, but in the presence of an alumina-nickel oxide catalyst at 215–220° and a hydrogen pressure of 110 atmospheres it yields l-iso*camphane*, the reduction being preceded by dehydration.[**] With a copper oxide-nickel oxide catalyst under similar conditions only camphene is formed.

Characteristic of borneol is the facility with which it is oxidised to camphor. This oxidation can be effected by distillation over copper,[††] by passage of the vapour over Raney nickel at 350°,[‡‡] by the action of oxides of nitrogen or by treatment in light petroleum solution with ozone. With concentrated nitric acid, oxidation to camphoric acid occurs, although, if a weak acid is used, camphor can be obtained. Oxidation with chromic acid proceeds in an interesting manner. By treatment with this reagent of the mixture of bornyl and *iso*bornyl acetates prepared by the acetylation of the crude alcohol mixture resulting from the reduction of camphor, Schrötter* obtained a substance, $C_{12}H_{18}O_3$, which gave on hydrolysis a substance having the composition of a hydroxycamphor, $C_{10}H_{16}O_2$. The constitution of this hydroxycamphor has been determined by Bredt and Goeb.[†] By the preparation of an *acetyl* derivative, m.p. 76–77°, and a *semicarbazone*, m.p. 222–224°, they showed it to contain a hydroxy group and carbonyl group. On oxidation of the alcohol a diketone, d-*paradiketocamphane* (5-*ketocamphor*), m.p. 206·5–207°, $[\alpha]_D$ +103·42°, *disemicarbazone*, m.p. above 262°, was obtained, which must be represented by (XXI), since the possible isomeride (XXII), derived from 6-ketoborneol (XXIII) would be symmetrical and could not therefore be optically active. From this it follows that Schrötter's hydroxycamphor is actually d-6-*hydroxyepicamphor* (XXIV). This structure was supported by the fact that on oxidation no camphoric acid was obtained; on reduction with sodium and alcohol it gives a glycol, m.p. 233–234°, presumably 2:5-*dihydroxycamphane*. The diketone (XXI) has been prepared also by the oxidation of camphor (I) with chromic acid (see p. 394).

---

[*] Tafel and Schmitz, *Z. Elektrochem.* 1902, **8**, 288. [†] *J.C.S.* 1907, **91**, 1973.

[‡] Ikeda, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1927, **7**, 47.

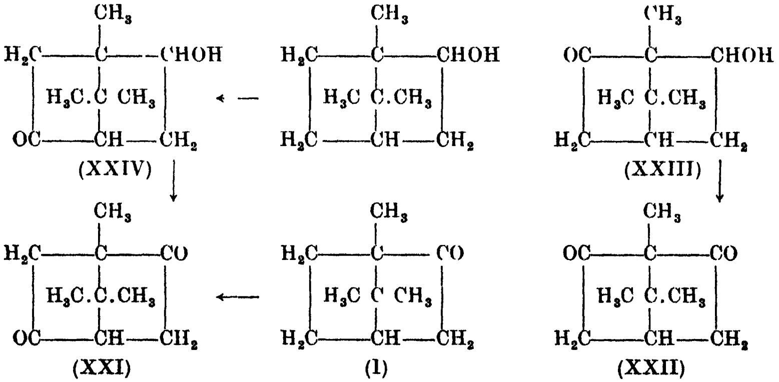
[§] *J.C.S.* 1934, p. 1773. [||] Vol. I, p. 243.

[¶] Almost identical physical constants, apart from the change in sign of rotation, were observed for the *l*-series.

[**] Ipatiev, *Ber.* 1912, **45**, 3207.

[††] Alby and Brustier, *Bull. Soc. chim.* 1911 [iv], **9**, 733; Neave, *J.C.S.* 1912, **101**, 513; Masumoto, *Mem. Coll. Sci. Kyoto*, 1925, **9**, 219; Christenson, Gilbert and Bocek, *J. Amer. C.S.* 1938, **60**, 2331.

[‡‡] Rutovski and Muliar, *J. Appl. Chem. Russ.* 1941, **14**, 173.



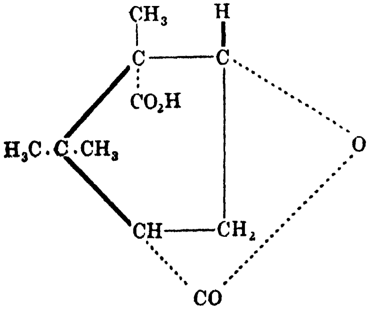
---

* *Monatsh.* 1881, **2**, 224.

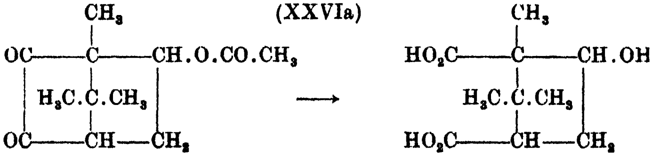
[†] *J. pr. Chem.* 1920 [ii], **101**, 273.

It was evident, however, that the hydroxycamphor, m.p. 248°, was not quite homogeneous, since, when it was regenerated from either its acetyl or benzoyl derivative, it melted at 237–238°. In a more recent investigation, Asahina, Ishidate, and Tsukamoto* have oxidised *l*-bornyl acetate with chromic acid, and have shown that the product, although mainly the acetate (m.p. 78°, $[\alpha]_D^{24^\circ}$ -88°) of *l*-6-hydroxyepicamphor (XXIV), also contains 6-acetoxycamphor, 6-ketocamphor (XXII) and l-6-*acetoxycamphorquinone* (XXV), m.p. 109°, $[\alpha]_D^{23^\circ}$ -191°. This quinone was also prepared by direct oxidation of the acetate of (XXIV) with selenium dioxide; on further oxidation with alkaline hydrogen peroxide it gives d-5-*hydroxycamphoric acid* (XXVI), m.p. 165°, $[\alpha]_D^{21^\circ}$ $+8^\circ$ (in alcohol).

According to Toivonen (private communication) this 5-hydrocamphoric acid, unlike the stereoisomer derived from *iso*borneol (see below), readily forms a *lactonic acid*, to which the formula (XXVIa) must be assigned, since the formation of a lactone indicates that the hydroxyl and carboxyl groups must be on the same side of the *cyclo*pentane ring; it follows, therefore, that in borneol the hydroxyl group must be *trans*- to the *gem*-dimethyl bridge, and that the alcohol consequently has the *endo*-structure (compare p. 357).



(XXVIa)



(XXV) (XXVI)

---

* *Ber.* 1936, 69, 349.

It was originally stated that *iso*bornyl acetate was resinified by chromic acid, but more recently Toivonen and Halonen[*] have shown that under carefully controlled conditions it gives products similar to those obtained from bornyl acetate. Thus, *dl-iso*bornyl acetate gives what is probably a mixture of the acetates of dl-5- and dl-6-*keto*iso*borneols* (stereoisomers of (XXIV) and (XXIII) respectively), since on further oxidation, with selenium dioxide, dl-5:6-*diketo*iso*bornyl acetate*, m.p. 103–104° [stereoisomer of (XXV)] was obtained, which with alkaline hydrogen peroxide gave dl-5-*hydroxycamphoric acid*, m.p. 205–207°.

When borneol is oxidised with ferric chloride in ethereal solution in the presence of sunlight, camphor is formed; if *iso*borneol be similarly treated no camphor is obtained, but Puxeddu's conclusion[†] that they must therefore have a different structure is not justified.

Borneol is oxidised by chlorine to camphor both in the presence and absence of water; with bromine in light petroleum solution, however, an unstable additive compound, $C_{10}H_{18}O, Br_2$, can be prepared.[‡] This derivative is decomposed immediately by either alcohol or alkali yielding a mixture of borneol and camphor. Similar unstable additive compounds are obtained also with hydrogen bromide and hydrogen iodide in light petroleum solution. Its conversion into the bornyl halides has been discussed already (p. 342).

Unlike *iso*borneol, borneol is comparatively stable to dehydrating agents although, according to Aschan,[§] this difference is not so marked as is generally assumed. It is not attacked when warmed with zinc chloride in benzene solution nor by dilute sulphuric acid, but with 50 per cent. sulphuric acid a good yield of camphene, accompanied by some *dibornyl* ether, b.p. 312–314°/760 mm. is obtained.[‖] Camphene is also obtained by digestion with potassium hydrogen sulphate[¶] by heating under pressure with aqueous magnesium chloride solution[**] and by dehydration in the vapour phase over thoria at 350°.[††] When borneol is fused with potassium hydroxide at 250–280° under pressure, ring fission occurs with the formation of *campholic acid* (XXVII).[*]

---

[*] *Suomen Kem.* 1946, **19** B, 1.

[†] *Gazzetta*, 1929, **59**, 59.

[‡] Wallach, *Annalen*, 1885, **230**, 226.

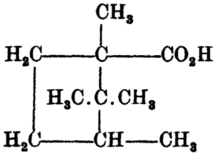
[§] *Annalen*, 1911, **383**, 11.

[‖] Konowalov, *J. Russ. Phys. Chem. Soc.* 1900, **32**, 76; Gobulov, *ibid.* 1912 **44**, 1061.

[¶] Wallach, *Annalen*, 1885, **230**, 237.

[**] Ipatiev and Pines, *J. Amer. C.S.* 1944, **66**, 1120.

[††] Brus and Bruster, *Bull. Inst. Pin*, 1934, p. 99.



(XXVII)

Borneol reacts readily with sodium to give the corresponding sodium derivative, the preparation of which can be carried out most conveniently by allowing the reaction to proceed in a neutral solvent. The sodium derivative can be used with advantage for the preparation of bornyl ethers and esters, of which a large number are known, and which have been used extensively in the study of problems in the field of optical rotatory power and dispersion.[†]

The bornylurethanes are not suitable for the characterisation of borneol, since, according to Bertram and Walbaum,[‡] both bornyl and *iso*bornyl *phenylurethanes* melt at 138–139°; the *α-naphthylurethanes*, which were prepared by Neuberg and Hirschberg,[§] also show little difference in their melting-points, which are 132° and 129° respectively.

Whilst a detailed consideration of the bornyl esters lies outside the scope of this book, mention must be made of *methyl bornylxanthate, d-* and *l-*, m.p. 56–57°, $[\alpha]_D$ +33·69°, −33·38°, *dl-*, m.p. 28·5–29°, since on distillation it yields bornylene (see p. 324).[||] The preparation of this ester has been suggested by Tschugaev[¶] as a convenient method for the separation of borneol and *iso*borneol, since, whereas methyl bornylxanthate on hydrolysis yields borneol, methyl *iso*bornylxanthate is dehydrated to camphene. This tendency for dehydration in place of hydrolysis to occur is shown also by d-*bornyl toluene*-p-*sulphonate,* m.p. 67°, $[\alpha]_D$ +26·34°, which on warming with sodium ethoxide yields camphene.[*] d-*Bornyl-β*-d-*glucoside*, m.p. 154–155°, $[\alpha]_D^{20^\circ}$ $-15{\cdot}2^\circ$ (in alcohol) and l-*bornyl-β*-d-*glucoside*, m.p. 135–136°, $[\alpha]_D^{21^\circ}$ $+55{\cdot}6^\circ$ (in alcohol) have been described by Lipschitz and Buding.[†]

---

[*] Guerbet, *Compt. rend.* 1909, **148**, 720; *Bull. Soc. chim.* 1909 [iv], **5**, 415.

[†] *Inter al.*, Pickard and Kenyon, *J.C.S.* 1915, **107**, 35; Kenyon and Priston, *ibid.* 1925, **127**, 1472.

[‡] *J. pr. Chem.* 1894 [ii], **49**, 5.

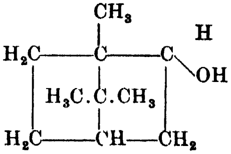
[§] *Biochem. Z.* 1910, **27**, 344.

[||] Tschugaev, *J. Russ. Phys. Chem. Soc.* 1904, **36**, 988.

[¶] Compare Pickard and Littlebury, *J.C.S.* 1907, **91**, 1973.

According to Harazsti[‡] *thioborneol*, m.p. 113°, accompanied by traces of *thiocamphor*, m.p. 125–130°, and *bornyl disulphide*, m.p. 195°, are formed by the action of sulphur on bornyl magnesium bromide (see also p. 446).

ISO*BORNEOL*



*iso*Borneol does not occur in nature, but since it is always formed together with borneol either by the hydration of camphene or by the action of sodium on camphor, it has been known since about 1859 (compare p. 350). The constitution of *iso*borneol and its relationship to borneol has been discussed already (p. 353).

*iso*Borneol is readily prepared by the hydration of camphene with acetic-sulphuric acid mixture,[§] the *iso*bornyl acetate so obtained yielding, on hydrolysis, an *iso*borneol which is almost completely racemised.[||] The conversion may also be brought about by sulphuric acid in ethereal solution, the reaction then proceeding with the intermediate formation of the sulphate ester; the use of *iso*amyl ether is said to be particularly effective.[¶] A more convenient method has, however, been described by Vavon and Peignier,[**] who have shown that camphor, on catalytic hydrogenation in the presence of platinum black, gives *iso*borneol in a yield of about 80 per cent. The separation of the optically pure forms of the alcohol can be carried out by the method adopted by Pickard and Littlebury.[*] *l-iso*Bornyl hydrogen phthalate was purified by the crystallisation of its *l*-menthylamine salt, *d-iso*bornyl hydrogen phthalate being separated in the form of its cinchonine salt. The corresponding *d*- and *l*-alcohols were obtained on hydrolysis of the hydrogen phthalates.

---

[*] Ferns and Lapworth, *J.C.S.* 1912, **101**, 278; compare Patterson and McAlpine, *ibid.* 1928, p. 2471; Huckel, Tappe and Legutke, *Annalen*, 1940, **543**, 191.

[†] *Compt. rend.* 1937, **205**, 58.

[‡] *J. pr. Chem.* 1937 [ii], **149**, 301.

[§] Bertram and Walbaum, *J. pr. Chem.* 1894 [ii], **49**, 1.

[||] Beckmann, *J. pr. Chem.* 1897 [ii], **55**, 39; *Ber.* 1909, **42**, 491.

[¶] Schwalbe and Aschan, *Finsk. Kem. Medd.* 1932, **40**, 133; **41**, 98.

[**] *Bull. Soc. chim.* 1924 [iv], **35**, 925.

*iso*Borneol can be best characterised and distinguished from borneol by the preparation of the p-*nitrobenzoate*, which melts at 129°.[†]

Pickard and Littlebury found *d*- and *l-iso*borneols to melt at 214°, although the somewhat higher melting-point, 217°, has been recorded by Henderson and Heilbron. The optically active *iso*borneols differ from the borneols, in that their rotatory power shows marked variations depending upon the nature of the solvent in which it is determined; concentration, however, has little effect. In ethyl acetate solution Pickard and Littlebury observed $[\alpha]_D$ +34·09°, −34·34°, whilst in toluene solution the value $[\alpha]_D$ +21·32° was found. Darmois[‡] has made use of the rotatory dispersion of solutions of borneol and *iso*borneol for the determination of the composition of mixtures of the two alcohols.

In addition to the methods mentioned above, *iso*borneol is obtained by any of the general methods used for the preparation of borneol (pp. 350–353).

In its reactions *iso*borneol resembles borneol, although the greater facility with which it undergoes dehydration to camphene causes it to exhibit slight differences. Its reduction to *iso*camphane by moist zinc dust has already been commented upon (p. 275). This hydrocarbon is obtained also by reduction with hydrogen under high pressure using an alumina-nickel oxide catalyst, camphene being obtained with a copper oxide-alumina catalyst[§] (compare p. 276).

*iso*Borneol differs from borneol in not being oxidised to camphor when distilled over copper,[‖] the oxidation proceeding smoothly, however, by the action of air (or oxygen) in the presence of various catalysts. Owing to its technical importance, the catalytic oxidation of the alcohol has been very thoroughly studied and satisfactory results are obtained in toluene solution by the use of an iron oxide-nickel catalyst.[*] It should be mentioned that *d*-*iso*borneol gives on oxidation *l*-camphor, and *l*-*iso*borneol, *d*-camphor. Oxidation of *iso*borneol to camphor also occurs when the alcohol is subjected to the action of ozone, oxides of nitrogen, nitric acid and potassium permanganate. The oxidation of *iso*bornyl acetate with chromic acid has been described on p. 361. According to Ikeda and Fujita[†] a *keto*iso*bornyl acetate*, b.p. 150–155°/10 mm., *semicarbazone*, m.p. 187°, is formed when *iso*bornyl acetate is ozonised in acetic acid solution. On hydrolysis, a *keto*iso*borneol*, *semicarbazone*, m.p. 227°, is obtained, but its constitution and relationship to the other hydroxycamphors (p. 427) does not appear to have been determined.

---

[*] *J.C.S.* 1907, **91**, 1978.

[†] Henderson and Heilbron, *Proc. C.S.* 1913, **29**, 281.

[‡] *Ann. Chim.* 1911 [viii], **22**, 546.

[§] Ipatiev, *Ber.* 1912, **45**, 3207.

[‖] Neave, *J.C.S.* 1912, **101**, 513.

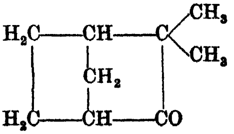
*iso*Borneol is oxidised by chlorine to camphor, whilst by the action of the halogen acids and phosphorus halides the *iso*bornyl halides can be prepared (p. 346). On fusion with potassium hydroxide *iso*borneol, like borneol, yields campholic acid (see p. 364).

The preparation of the esters and ethers of *iso*borneol can be carried out very conveniently from the sodium derivative, the risk of isomeric change being thereby minimised. In this manner, Meerwein and Gerard[‡] prepared iso*bornyl methyl ether*, b.p. 191°, d_4^{20} 0·9250, $n_D^{20°}$ 1·4625.

A large number of *iso*bornyl esters have been described and have been utilised more especially in the study of problems related to rotatory dispersion (compare p. 359).

C. KETONES

CAMPHENILONE



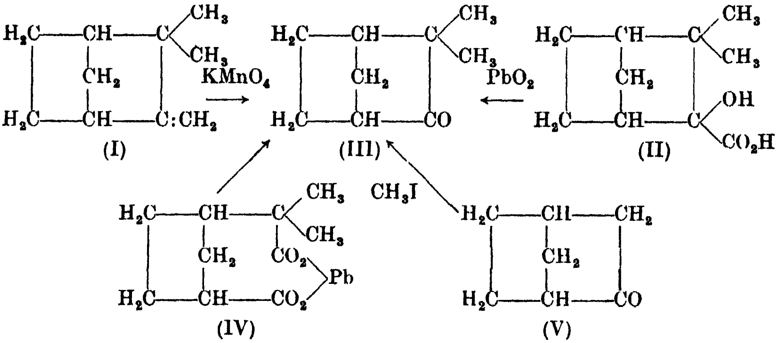
---

[*] Compare Aschan, *Naphtenverbindungen, Terpene und Campherarten*, pp. 168–173.

[†] *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1927, 7, 12.

[‡] *Annalen*, 1924, **435**, 174.

Camphenilone (III) was first separated by Wagner[*] during his investigation of the oxidation of camphene (I) with potassium permanganate (p. 297), and he showed also that it was obtained when camphenylic acid (II) was oxidised with lead peroxide.



The formula assigned by Wagner to camphenilone was confirmed by Komppa and Hintikka's[†] synthesis of the ketone by the distillation of the lead salt of camphenic acid (IV); Diels and Alder[‡] have also synthesised it by the methylation of *norcamphor* (V) with methyl iodide in the presence of sodamide.

Camphenilone can be prepared most readily by the oxidation of ω-nitrocamphene (VI) (p. 312) with potassium permanganate.[§] Attention must also be directed to its formation by the ozonolysis of the acetate of the enolic form of camphenilanaldehyde (VII)[‖] and to its preparation by Lipp[¶] from *tricyclenic acid* (VIII) in a somewhat unusual manner. When the amide of this acid is converted by Jeffrey's method into the urethane and the latter fused with alkali, the *amine* (IX) is only obtained in a very small yield, camphenilone (III) and the corresponding secondary alcohol, camphenilol, forming the main products of the reaction.

---

[*] *J. Russ. Phys. Chem. Soc.* 1896, **28**, 64; 1897, **29**, 124; compare *inter al.*, Aschan, *Annalen*, 1911, **383**, 44.

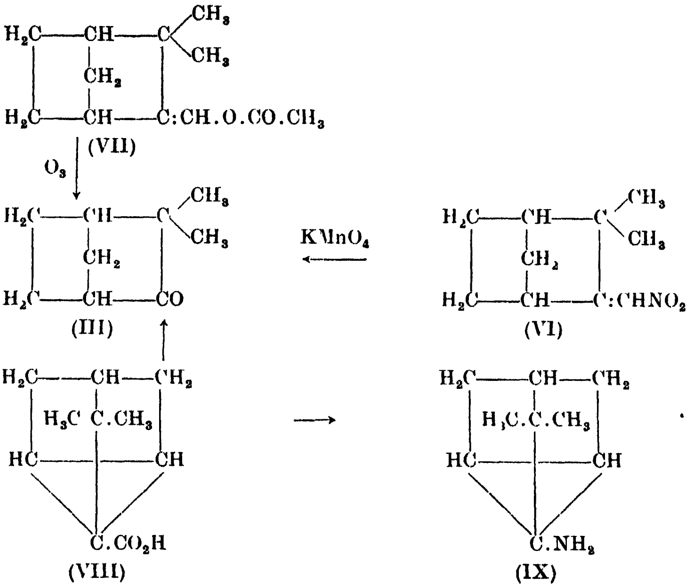
[†] *Ber.* 1914, **47**, 1550.

[‡] *Annalen*, 1929, **470**, 63; 1931, **486**, 202.

[§] Jagelki, *Ber.* 1899, **32**, 1498; Blaise and Blanc, *Compt. rend.* 1899, **129**, 886; *Bull. Soc. chim.* 1900 [iii], **23**, 164; Komppa and Hintikka, *Annalen*, 1912, **387**, 294.

[‖] Semmler, *Ber.* 1909, **42**, 963; compare, however, Huckel and Hartmann, *Ber.* 1937, **70**, 962; Hückel, *Chem. Ber.* 1947, **80**, 41.

[¶] *Ber.* 1921, **54**, 1316.



Camphenilone can be most readily identified by the preparation of the *semicarbazone*, m.p. 224°, though according to Huckel and Hartmann* such identification should be confirmed by analysis of the derivative, since a mixed melting-point determination may be unsatisfactory.

dl-Camphenilone, which has a strong camphoraceous odour, melts at 38°, b.p. 195°, 73–75°/10 mm., d^{38} 0·9705, n_D 1·469; *d*-camphenilone has m.p. 38–39°, b.p. 193°, 78°/12 mm., $[\alpha]_D^{24^\circ}$ $+70{\cdot}4^\circ$ (in alcohol).† Dulou‡ has suggested the use of camphenilone as a solvent for molecular weight determinations, since it possesses the high freezing-point depression constant, *K* 605°.

On reduction, the secondary alcohol, *camphenilol*, is obtained, which exists in two stereoisomeric modifications. By the use of sodium and alcohol as the reducing agent, *l*-camphenilone gives l-*camphenilol* I, m.p. 76–77°, $[\alpha]_D^{20^\circ}$ -23° (in alcohol), which gives an *acid phthalate*, m.p. 146–147°, $[\alpha]_D^{19^\circ}$ -73° (in benzene) and a p-*nitrobenzoate*, m.p. 96–98°, $[\alpha]_D^{20^\circ}$ -42° (in benzene), whilst hydrogenation in acetic acid solution gives a product from which may be obtained *camphenilol* II, m.p. 151–153·5°, $[\alpha]_D^{20^\circ}$ +3° (p-*nitrobenzoate,* m.p. 97–99°), probably not stereochemically pure.[*]

---

* *Ber.* 1937, **70**, 962.

† Hückel, *Annalen,* 1941, **549**, 186; compare Aschan, *ibid.* 1915, **410**, 223.

‡ *Bull. Inst. Pin,* 1934, **54**, 210.

When the reduction is carried out with sodium in ethereal solution a *pinacone*, $C_{18}H_{20}O_2$, m.p. 134°, is formed. It has been suggested by Komppa and Hintikka[†] that this is a mixture of the two isomeric pinacones, m.p. 173–173·5° and 172·5–173°, which were prepared by Moycho and Zienkowski[‡] by the action of sodium and amyl formate on the ketone. Camphenilol reacts with phosphorus pentachloride to give *camphenilyl chloride,* m.p. 54°, b.p. 70–76°/15 mm.[§] It appears from the work of Komppa and Nyman[‖] that this chloride is not a true derivative of camphenilol, but probably consists mainly of *apobornyl chloride* (X), rearrangement having occurred during its preparation, similar to that observed with camphene hydrochloride; on saponification, it gives a mixture of camphenilol, apoborneol (*α-fenchocamphorol,* p. 542), and *β-fenchocamphorol,*[¶] and, on treatment with sodium phenoxide, *apobornylene* (XI) is obtained. If, on the other hand, the hydrogen chloride is removed by treatment with aniline, the product is a mixture of *santene* (XIII) and *apocyclene* (p. 331).[**] Since ordinary apobornyl chloride has not been found to give santene on treatment with aniline,[††] this would appear to indicate that the production of santene, possibly through the intermediate formation of camphenilyl chloride (XII), can only occur from the other stereoisomeric form of apobornyl chloride. A similar instance has been encountered in the formation of α-methylsantene, which can be obtained by the dehydration of α-fenchyl alcohol, but not from the stereoisomeric β-alcohol (see p. 536). Reference has already been made (p. 246) to the formation of santene by dehydration of camphenilol with potassium hydrogen sulphate.

---

[*] Hückel and Tappe, *Ber.* 1936, **69**, 2769; compare Komppa and Beckmann, *Annalen,* 1936, **522**, 137; Hückel, *ibid.* 1941, **549**, 186.

[†] *Annalen,* 1912, **387**, 294.

[‡] *Ibid.* 1905, **340**, 55.

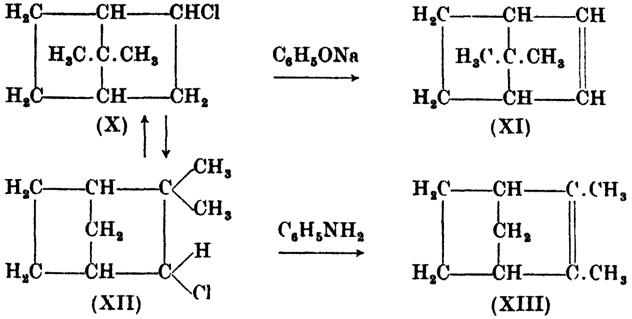
[§] Jagelki, *Ber.* 1899, **32**, 1503; Hintikka and Komppa, *Annalen,* 1912, **387**, 294; *Bull. Soc. chim.* 1917 [iv], **21**, 14.

[‖] *Ber.* 1936, **69**, 1813.

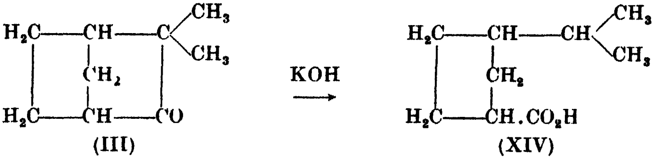
[¶] A similar mixture is obtained when *camphenilylamine* is treated with nitrous acid (Komppa and Komppa, *Ber.* 1936, **69**, 2606).

[**] Gratton and Simonsen, *J.C.S.* 1935, p. 1621.

[††] Komppa and Hasselström, *Annalen,* 1932, **497**, 116.



Camphenilone is extremely resistant to oxidising agents although, according to Nametkin,[*] it yields *iso*camphoronic acid on digestion with dilute nitric acid. Fission of the dicyclic ring can, however, be effected either by the action of sodamide in benzene solution[†] or on fusion with potassium hydroxide,[‡] when *β-dihydrocamphoceenic acid* (XIV), b.p. 140–141°/15 mm., $d_{4°}^{20°}$ 0·9820, n_D 1·4565, or with the first reagent, the *amide*, m.p. 168°, is obtained. The latter has been synthesised by Bouveault and Blanc.[§]



Camphenilone reacts with phosphorus pentachloride in chloroform solution to give a *dichloride*, m.p. 174°,[‖] from which, by the action of sodium, apobornylene and apocyclene can be obtained (see p. 331).

Campheniloneoxime (XV), which was first prepared by Wagner[¶] and subsequently by other investigators,[**] melts at 105–107°, b.p. 128–129°/14 mm.; the *d*-form has m.p. 123°, $[\alpha]_D^{20°}$ +160° (in benzene).[††] On digestion with dilute sulphuric acid it yields, in addition to camphenilone, the *nitrile* of *camphoceenic acid* (XVI), b.p. 85–90°/10 mm.,[*] which gives on hydrolysis the corresponding *acid*,[*] m.p. 54°. This nitrile also results in a somewhat better yield when the oxime is warmed with acetyl chloride, some *campheniloneisooxime* (XVII) being formed simultaneously.

---

[*] *Annalen*, 1924, **438**, 193.

[†] Semmler, *Ber.* 1906, **39**, 2580.

[‡] Hintikka, *Annal. Acad. Sci. Fennicae*, 1913, III A, **9**, 1.

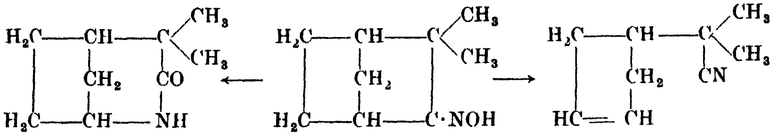
[§] *Compt. rend.* 1908, **147**, 1315.

[‖] Moycho and Zienkowski, *Annalen*, 1905, **340**, 56; Hintikka and Komppa, *Annalen*, 1912, **387**, 294; Komppa and Roschier, *ibid.* 1922, **429**, 175.

[¶] *J. Russ. Phys. Chem. Soc.* 1896, **28**, 76; *Bull. Soc. chim.* 1896 [iii], **16**, 1837.

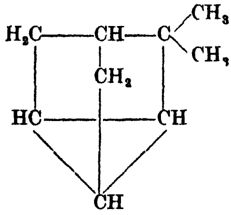
[**] Compare Komppa, *Annalen*, 1909, **366**, 75.

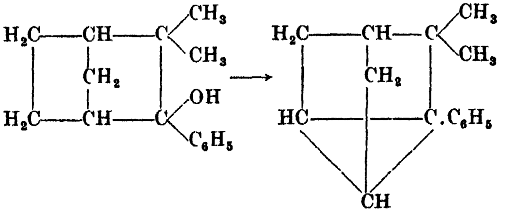
[††] Hückel, *Annalen*, 1941, **549**, 186.


(XVII) (XV) (XVI)

Camphenilonehydrazone, m.p. 27–28°, b p. 103°/8 mm., $[\alpha]_D^{20^\circ}$ $+223^\circ$ (in alcohol), on reduction with sodium ethoxide gives the saturated hydrocarbon *camphenilane* (p. 278), whilst on oxidation with mercuric oxide in alcoholic alkali it gives *apocyclene* (XVIII), m.p. 42°.

Reference has been made already (p. 317) to the action of methyl magnesium iodide on camphenilone, when methylcamphenilol is obtained. The corresponding phenyl derivative, *phenylcamphenilol* (XIX), b.p. 122°/4 mm., has been prepared by Aschan[†] and by Bredt-Savelsberg[‡] by the action of phenyl magnesium bromide on the ketone. On dehydration it yields a tricyclic hydrocarbon, b.p. 96–97°/5 mm., $d_4^{10\cdot5^\circ}$ 1·0060, $n_D^{10\cdot25^\circ}$ 1·5471, which is probably represented by (XX).


(XVIII)


(XIX) (XX)

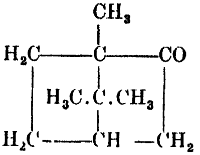
---

[*] Jagelki, *Ber.* 1899, **32**, 1505; Blaise and Blanc, *Compt rend.* 1899, **129**, 888; *Bull. Soc. chim* 1900 [iii], **23**, 174; Semmler, *Ber* 1909, **42**, 249.

[†] *Annalen*, 1915, **410**, 223.

[‡] *Ber.* 1923, **56**, 554.

CAMPHOR



The dicyclic ketone, *camphor*, $C_{10}H_{16}O$, which does not occur very widely distributed in nature, has been found in the *d*-, *l*- and *dl*-forms. The main source of *d*-camphor is the wood of the tree, *Cinnamomum camphora* Nees, which is found from Cochin-China to Shanghai and in the islands from Hainan to Southern Japan, that is between 10° to 34° North Latitude. The most extensive forests are those in Formosa, where the climate is moist and tropical to subtropical. It has been successfully cultivated in India, Burma, Ceylon, the Malay States, Java, Australia, East and South Africa, Italy, Algiers, Florida, California, Brazil, the West Indies, Mauritius and Madeira. Although camphor was obtained originally from China, the main source of natural camphor is now Formosa. Camphor is present in all parts of the tree and, whilst the percentage is highest in the trunk, it has been suggested that the leaves might in certain cases also be utilised.* *l*-Camphor has been separated from the oil prepared from the leaves of *Blumea balsamifera* and also from the oils of *Artemisia tridentata* and *Lavandula pedunculata*,† whilst *dl*-camphor has been obtained from the oil of *Chrysanthemum sinense* var. *japonicum*.

Owing to the ease with which it can be isolated and to its remarkable properties, camphor has been known and valued for medicinal purposes in the Far East (China and Japan) from the earliest times. It is not referred to in Greek or Roman literature and it would appear to have been introduced into Europe by the Arabs under the name *Káfár* (from the Sanskrit *Kapūra*, meaning "white"). The true Chinese camphor was for a long time confused with borneol, borneocamphor, which was obtained from Sumatra and which was considered to be of greater medicinal value. In the West, much confusion also reigned as to the source of camphor, and it was at one time considered to be a mineral resin.

---

* Compare *inter al.*, Howard, Robertson and Simonsen, *Ind. For. Rec.* 1923, **9**, 307.

† Adams and Oakberg, *J. Amer. C.S.* 1934, **56**, 457; Gattefossé and Igolen, *Compt. rend.* 1942, **214**, 885.

In view of its medicinal value the action of various reagents on camphor was studied by the alchemists. Thus Libavius[*] refers to the solution of camphor in nitric acid and Kosegarten[†] prepared by the action of this reagent an acid, which was undoubtedly camphoric acid. Robert Boyle[‡] observed that camphor could be precipitated unchanged from solution in sulphuric acid. In the determination of the origin of camphor the analysis carried out by Lavoisier was of great importance, since he showed that it contained only carbon, hydrogen and oxygen. The composition and the molecular weight were first determined by Dumas[§] and by Blanchet and Sell,[‖] who showed it to have the formula $C_{10}H_{16}O$. Prior to this its physical constants had been determined with some accuracy, whilst Biot[¶] had observed that its vapour was optically active. Some years later camphoric acid and camphoric anhydride were shown to have the formulae $C_{10}H_{16}O_4$ and $C_{10}H_{16}O_3$ respectively.[**] In 1841 Pelouze[††] made the very important observation that borneocamphor, borneol, which had the formula $C_{10}H_{18}O$, gave on oxidation ordinary camphor. This was confirmed by Gerhardt,[‡‡] who suggested that camphor was the aldehyde corresponding to the alcohol borneol. Two other observations, which were later to become of considerable importance, were made at this time by Delalande,[§§] who found that by distillation over lime camphor gave campholic acid, whilst on treatment with dehydrating agents, such as zinc chloride or phosphorus pentoxide, *p*-cymene was obtained.

The experiments referred to above were all carried out with *d*-camphor, the laevorotatory form being first separated in 1848 by Dessaignes and Chautard[*] from the oil of *Matricaria Parthenium* L.

---

[*] *Alchymia*, 1595.

[†] *Dissertatio de Camphora et partibus quae eam constituunt*, 1785.

[‡] *The Origin of Formes and Qualities*, 2nd ed. 1667, Section II, p. 183.

[§] *Ann. Chim.* 1833 [ii], **48**, 430; *Annalen*, 1833, **6**, 245.

[‖] *Annalen*, 1833, **6**, 302.

[¶] *Mém. de l'Academie*, **2**, 114; **13**, 144.

[**] Malaguti, *Annalen*, 1837, **22**, 32; Liebig, *ibid.* p. 50; Laurent, *ibid.* p. 135.

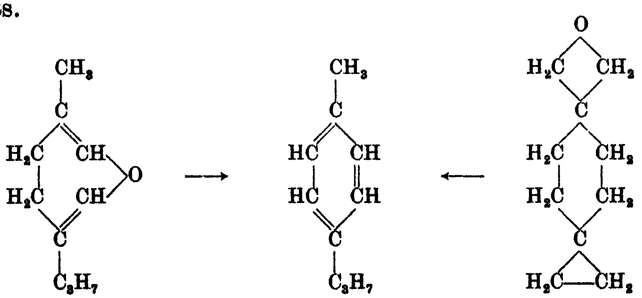
[††] *J. Pharm.* 1841, **26**, 645; *Annalen*, 1841, **40**, 328.

[‡‡] *Annalen*, 1843, **45**, 29.

[§§] *Ibid.* 1841, **38**, 337.

Gerhardt's suggestion that camphor was the aldehyde corresponding to borneol received apparent support from the experiments of Berthelot,[†] who showed that, when it was heated in a sealed tube at 180–200° with an alcoholic solution of sodium hydroxide, borneol was obtained, whilst in addition an acid, "camphinic acid", was formed. To this acid Berthelot erroneously gave the formula $C_{10}H_{16}O_2$, and he regarded the reaction which had occurred as a Cannizzaro reaction, analogous to the conversion of benzaldehyde into benzyl alcohol and benzilic acid. Tollens and Fittig[‡] and Weyl[§] considered that camphor was probably a ketone, since it was not oxidised by chromic acid to an acid having the formula $C_{10}H_{16}O_2$, nor could it be reduced readily. This latter argument, however, lost its force when Baubigny[‖] showed that it could be reduced with sodium in alcoholic solution. Direct evidence of the presence of a carbonyl group was lacking, and in 1870 Meyer[¶] and Hlasiwetz[**] suggested the possibility of its being an oxide.

The Meyer formula (I) and the Hlasiwetz formula (II) mark an epoch in the history of the chemistry of camphor. As will be obvious, they are based on the Kekule benzene formula, and are an attempt to correlate the constitution with that of cymene (III),[††] into which it can be converted by the action of dehydrating agents.



---

[*] *J. Pharm.* 1848 [iii], **13**, 241; *Compt. rend.* 1853, **37**, 166.

[†] *Annalen*, 1859, **110**, 367.

[‡] *Ibid.* 1864, **129**, 371.

[§] *Ber.* 1868, **1**, 94.

[‖] *Compt. rend.* 1866, **63**, 221.

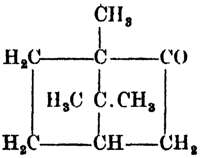
[¶] *Ber.* 1870, **3**, 116.

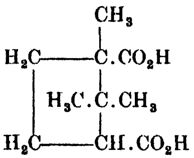
[**] *Ibid.* p. 539.

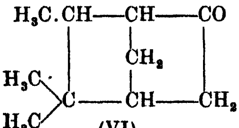
[††] The actual constitution of *p*-cymene was not known at the time (see Vol. I, p. 145).

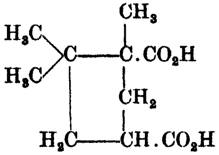
In the following years a great variety of formulae (more than thirty)[*] were suggested for camphor and camphoric acid, but since these are now only of historic interest it would be of little value to discuss them in detail. It is doubtful if, in the whole range of organic chemistry, any two substances have been the subject of such intensive study, and the difficulties encountered in the determination of their constitution has been due mainly to their tendency to undergo intramolecular rearrangements.

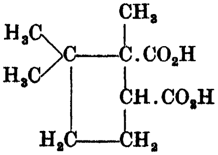
In 1893 Bredt suggested that the majority of the reactions of camphoric acid could be simply explained, if the acid were the *cyclo*pentane acid (V), when camphor would be represented by (IV). Although the subsequent synthetical investigations of Komppa and of Perkin and Thorpe have shown Bredt's formulae to be correct, they did not receive general acceptance and various modifications were proposed. Amongst these the most important were due to Tiemann[†] (VI), Perkin[‡] (VII) and Perkin[§] and Bouveault[‖] (VIII).


(IV)


(V)


(VI)


(VII)


(VIII)

---

[*] A full account of the early formulae assigned to camphor has been given by Aschan in his monograph *Die Constitution des Camphers und seine wichtigsten Derivative*. The following are some of the most important references in the literature: Kachler, *Annalen*, 1872, **164**, 92; 1873, **169**, 185; Wreden, *Ber.* 1872, **5**, 765, 1106; 1877, **10**, 714; Bruylants, *ibid.* 1878, **11**, 451; Armstrong, *ibid.* p. 1698; Armstrong and Miller, *ibid.* 1883, **16**, 2260; Kanonnikov, *J. Russ. Phys. Chem. Soc.* 1883, **15**, 469; Bredt, *J. pr. Chem.* 1885 [ii], **32**, 511; Brühl, *Annalen*, 1888, **226**, 261; Collie, *Ber.* 1892, **25**, 1114.

[†] *Ber.* 1895, **28**, 1079.

[‡] *J.C.S.* 1898, **73**, 796.

[§] *Ibid.* 1898, **73**, 819.

[‖] *Bull. Soc. chim.* 1897 [iii], **17**, 990.

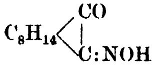
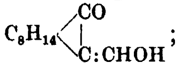
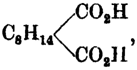
It will be as well to summarise here the conditions which must be satisfied by any constitutional formulae for camphor and camphoric acid.

(i) Camphor has the composition $C_{10}H_{16}O$ and camphoric acid, $C_{10}H_{16}O_4$, is a dibasic acid.

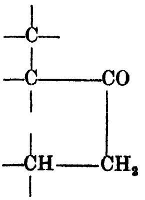
(ii) The molecular refractions of camphor and camphoric acid show them to be saturated, from which it follows that camphor must be dicyclic and camphoric acid monocyclic.[*]

(iii) Camphor and camphoric acid are both optically active and must therefore contain one centre of asymmetry. The Bredt formula for camphoric acid contains two such centres and both are present in camphor. For reasons to be discussed later (p. 384) the ketone can exist in only two optically active modifications.

(iv) Camphor is a ketone; (*a*) it gives an oxime[†] and a semicarbazone,[‡] and (*b*) it can be reduced with sodium and alcohol to the corresponding secondary alcohol, borneol.

(v) Camphor contains the grouping $—CH_2—CO—$, since it yields (*a*) on treatment with *iso*amyl nitrite, iso*nitrosocamphor*,  $C_8H_{14}<\begin{array}{l}CO\\ |\\ C{:}NOH\end{array}$;[§] (*b*) a *hydroxymethylene* derivative,[‖]  $C_8H_{14}<\begin{array}{l}CO\\ |\\ C{:}CHOH\end{array}$; and (*c*) on oxidation a dibasic acid, camphoric acid,  $C_8H_{14}<\begin{array}{l}CO_2H\\ CO_2H\end{array}$, in which the two carboxyl groups are not similarly situated, since two different series of hydrogen esters can be prepared.

(vi) Camphoric acid has only one hydrogen atom in the α-position to the carboxyl groups, since on bromination it yields a monobromo-acid.[¶]

(vii) Camphor must contain the grouping  since its sodium derivative (IX) yields with cyanogen *cyanocamphor* (X), and from this by hydrolysis *homocamphoric acid* (XI) can be prepared.* The constitution of the latter is proved by its synthesis from *α-campholide* (XIII), a reduction product of the *anhydride* of camphoric acid (XII).† Now homocamphoric acid gives on bromination a *monobromo* acid (XIV), from which by treatment with alkali hydrogen bromide can be eliminated with the formation of *dehydrohomocamphoric acid* (XV). Utilising the Bredt formulae for camphor and camphoric acid, these reactions are illustrated in the following scheme and establish conclusively the presence of the grouping shown in the skeleton formula given at the head of this section.

---

[*] Kanonnikov, *J. pr. Chem.* 1885 [ii], **32**, 503; Brühl, *Ber.* 1891, **24**, 3701.

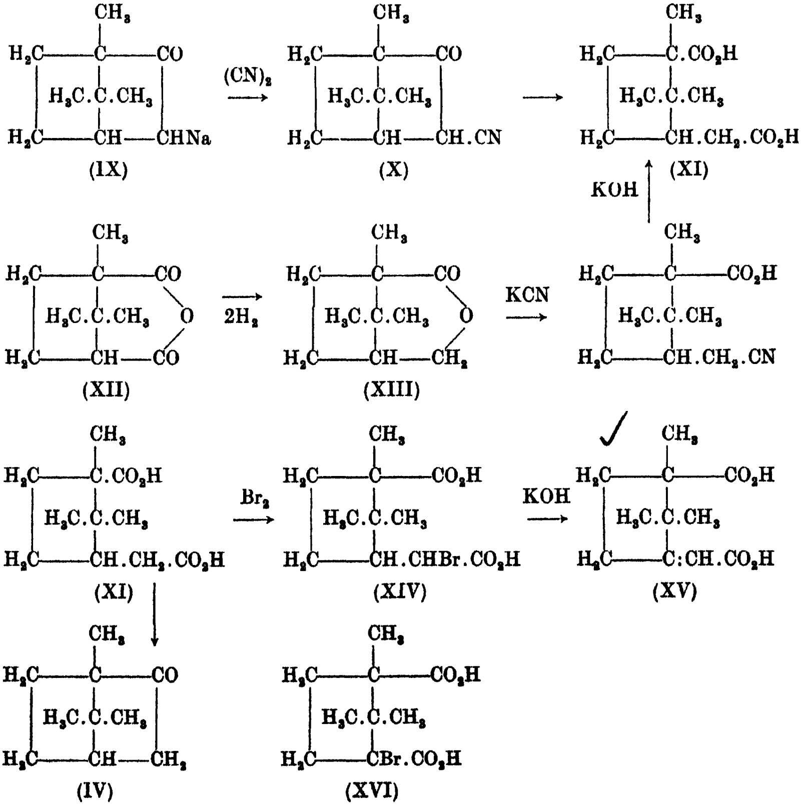
[†] Nägeli, *Ber.* 1883, **16**, 497.

[‡] Tiemann, *ibid.* 1895, **28**, 2191.

[§] Claisen and Manasse, *Annalen*, 1893, **274**, 79.

[‖] Claisen, Bishop and Sinclair, *ibid.* 1894, **281**, 314.

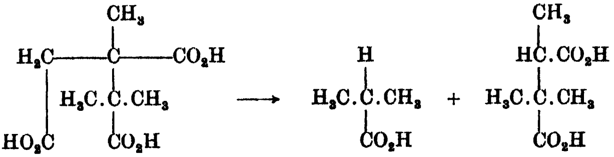
[¶] Aschan, *Ber.* 1893, **26**, 1640.



* Haller, *Compt. rend.* 1889, **109**, 68, 112; 1896, **122**, 446.
† Haller and Blanc, *ibid.* 1900, **130**, 376.

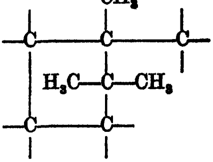
It will be observed that the hydrogen atom which is eliminated as hydrogen bromide from the monobromo acid (XIV) in the formation of dehydrohomocamphoric acid (XV) is the same as that which is substituted in the preparation of bromocamphoric acid (XVI) (see under (vi) above). It should be mentioned that by the distillation of the calcium salt of homocamphoric acid (XI) Haller[*] prepared camphor (IV).

(viii) By the oxidation of either camphor or camphoric acid with nitric acid the tribasic acid, *camphoronic acid*, $C_9H_{14}O_6$, is always obtained. This acid has been prepared synthetically by Perkin and Thorpe[†] and has been shown to be *αaβ-trimethyltricarballylic acid* (XVII), as had been suggested by Bredt.[‡] This suggestion of Bredt was the foundation of his formula for camphoric acid, and it was based essentially upon the fact that camphoronic acid on distillation at the ordinary pressure decomposed, yielding *iso*butyric acid (XVIII), trimethylsuccinic acid (XIX) and carbon dioxide.



(XVII) (XVIII) (XIX)

It follows from the formation of camphoronic acid that camphor and camphoric acid must contain the skeleton (XX). The recognition by Bredt of the correct formula for camphoronic acid was of fundamental importance, since it showed for the first time that the *iso*propyl group, appearing in such degradation products as *p*-cymene, formed part of the ring structure of the parent ketone.



(XX)

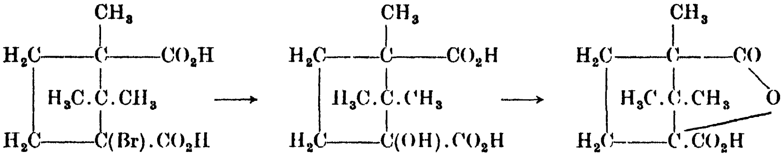
---

[*] *Compt. rend.* 1896, 122, 446; compare Bredt and Rosenberg, *Annalen*, 1896, 289, 1; Komppa, *Ber.* 1908, 41, 4470.

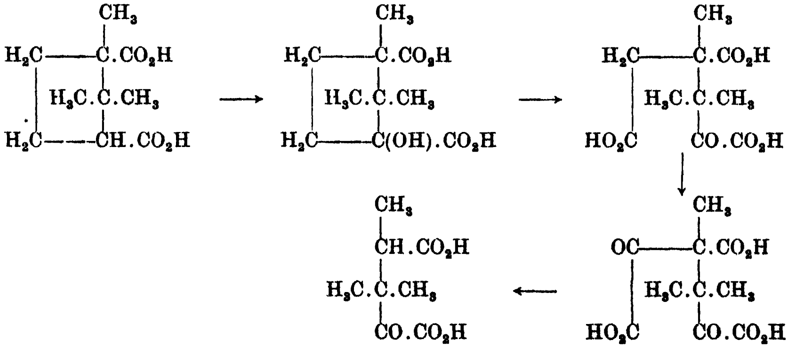
[†] *J.C.S.* 1897, 71, 1169.

[‡] *Ber.* 1893, 26, 3047.

(ix) Distillation of the calcium salt of homocamphoric acid yields camphor (see (vii) above); camphoric acid must therefore be a derivative of either glutaric or adipic acid, since, if it were a succinic acid derivative, a ring ketone would not be formed. It is in all probability a *substituted glutaric acid*, as the *hydroxy acid* (XXI) prepared from α-bromocamphoric acid (XVI) passes readily into a lactone, *camphanic acid* (XXII).


(XVI) (XXI) (XXII)

This view receives support from the observation of Balbiano,[*] that camphoric acid on oxidation with potassium permanganate yields amongst other substances a dibasic acid, $C_8H_{12}O_5$, generally known as Balbiano's acid. This acid, which gives on reduction with hydriodic acid αββ-trimethylglutaric acid, has been shown by Bardhan[†] to be the ketonic dibasic acid (XXIII), its formation from camphoric acid (V) being assumed by him to proceed in accordance with the scheme given below, although none of the intermediate products has been isolated and it presents many unusual features.


(XXIII)

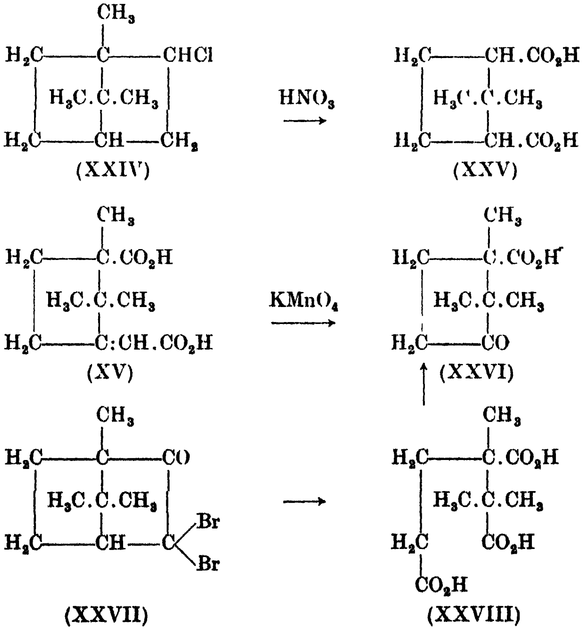
---

[*] *Ber.* 1897, **30**, 1901; 1899, **32**, 1017; *Gazzetta*, 1899, **29** [ii], 490; 1902, **32** [i], 485.
[†] *J.C.S.* 1928, p. 2604.

(x) Direct proof of the presence of a *cyclo*pentane ring structure in camphoric acid has been obtained in two ways.

(*a*) Bornyl chloride (XXIV) gives on oxidation with nitric acid *apocamphoric acid* (XXV)[*] and this acid has been prepared synthetically by Komppa.[†]

(*b*) Dehydrohomocamphoric acid (XV) gives on oxidation with potassium permanganate the ketonic acid, *camphononic acid*, $C_9H_{14}O_3$ (XXVI).[‡] This acid has also been prepared by an indirect method from *αα′-dibromocamphor* (XXVII). It was found by Lapworth and Chapman[§] that when this dibromide was oxidised with nitric acid in the presence of silver nitrate a tribasic acid, ***homocamphoronic acid***, $C_{10}H_{16}O_6$ (XXVIII), was obtained, the anhydride of which, when heated at 200–260°, gave camphononic acid (XXVI). For reasons to be discussed later, homocamphoronic acid must be represented by formula (XXVIII), its formation involving a molecular rearrangement.



---

[*] Gardner and Cockburn, *J.C.S.* 1898, **73**, 278.

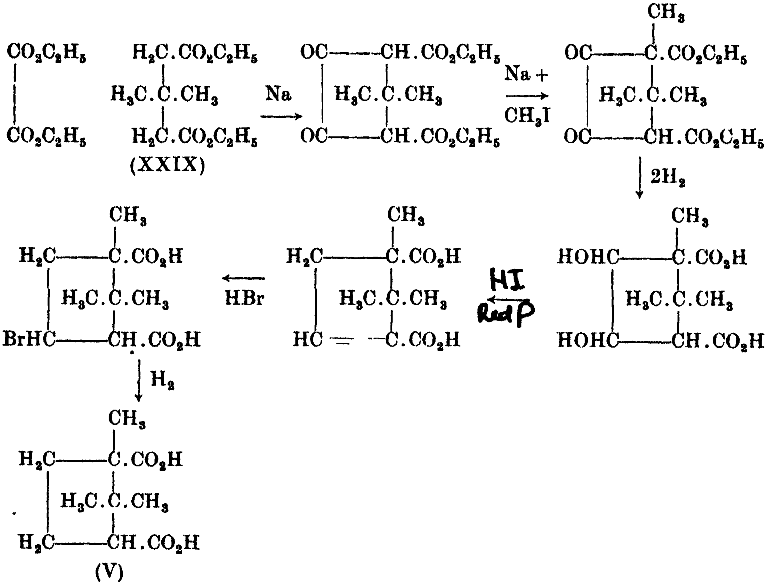
[†] *Ber.* 1901, **34**, 2472.

[‡] Lapworth, *J.C.S.* 1900, **77**, 1070.

[§] *J.C.S.* 1899, **75**, 986.

Since only adipic acids (or substituted adipic acids) are converted into ketones under the conditions used by Lapworth and Chapman, it follows that camphononic acid must contain a *cyclo*pentane ring.*

The Bredt formulae for camphor (IV) and camphoric acid (V), which account in a simple manner for all the reactions discussed above, have been confirmed by the synthesis of *dl*-camphoric acid, which was effected practically simultaneously by Komppa[†] and by Perkin and Thorpe.[‡] The Komppa synthesis, which involves a comparatively simple series of reactions, starts from *ethyl ββ-dimethylglutarate* (XXIX) and proceeds in accordance with the scheme:



The Perkin-Thorpe synthesis, which, like that of Komppa, leaves no doubt as to the constitution of the final product, involved very great experimental difficulties and the yield of the synthetic acid was extremely small. By the action of acetic

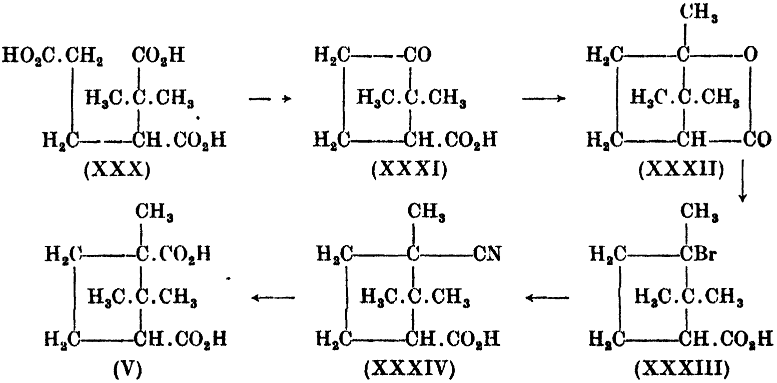
---

[*] A *cyclo*hexane derivative could result under the same conditions, but this is ruled out by other considerations, since homocamphoronic acid can be converted into camphoronic acid which is known to be ααβ-trimethyltricarballylic acid (p. 379).

[†] *Ber.* 1903, **36**, 4332; *Annalen*, 1909, **370**, 225.

[‡] *J.C.S.* 1904, **85**, 146; 1906, **89**, 799.

anhydride on the sodium salt of *αα-dimethylbutane-αβδ-tricarboxylic acid* (XXX) 2:2-*dimethyl*cyclo*pentan*-3-*one carboxylic acid* (XXXI) was prepared, the ethyl ester of which gave on treatment with methyl magnesium iodide *α-campholactone** (XXXII). From this, by the action of hydrogen bromide, 3-*bromo*-2:2:3-*trimethyl*cyclo*pentane carboxylic acid* (XXXIII) was prepared, which gave with potassium cyanide the *nitrile* (XXXIV). When this nitrile was hydrolysed, *dl*-camphoric acid (V) was obtained.



dl-Camphoric acid can be readily resolved into its optical enantiomorphs† and the two syntheses of the acid outlined above imply therefore a synthesis of *d*- and *l*-camphoric acids.‡ Further, since camphoric acid can be converted into camphor (p. 379), a complete synthesis of *d*-, *l*- and *dl*-camphors has been effected. The synthesis of *dl*-camphor also follows from that of *dl*-borneol described on p. 357.

Whilst the constitution of camphor has thus been rigidly established, it behaves in many of its reactions in an abnormal manner and some of the more important molecular rearrangements which it and its derivatives undergo will be discussed in the sequel.

Camphor can be readily identified by the preparation of the *oxime*, m.p. 119·5°, or the *semicarbazone*, m.p. 245°. The

---

* For a discussion of the constitution of this lactone and its conversion into α-campholytic acid see p. 504.

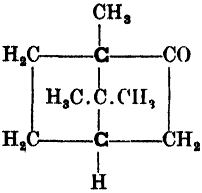
† Debierne, *Compt. rend.* 1899, **128**, 1112; Beckmann, *Ber.* 1909, **42**, 487.

‡ Komppa resolved his synthetic acid and converted the dextrorotatory modification into *d*-camphor.

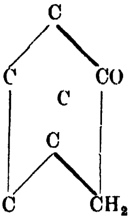
2:4-*dinitrophenylhydrazone* has m.p. 174°.* Since most of the derivatives of *d*-, *l*- and *dl*-camphor have the same melting-points, it is of interest to note that the *phenylsemicarbazones* show a marked difference, the *d*- and *l*- forms melting at 153–154° and the *dl*- at 171·5–172·5°.†

Camphor has a curious and very characteristic odour; it crystallises in thin plates and sublimes readily at the ordinary temperature. The *d*- and *l*- modifications melt at 178·5-179° and the *dl*- at 178-178·5°, b.p. 209·1°/759 mm., d_0^0 1·000. *d*-Camphor is optically active in the solid, liquid and gaseous phases and its rotatory power varies considerably with the nature of the solvent and with the concentration of the solution.‡ Thus, in absolute alcohol, the following values have been observed § $[\alpha]_D^{20°}$ +41·4° (*c*, 1); +43·6° (*c*, 5); +44·8° (*c*, 20), +48·4° (*c*, 50), and in 75 per cent. alcohol: $[\alpha]_D^{20}$ +34° (*c*, 1); +36·9° (*c*, 5); +39·8° (*c*, 20).

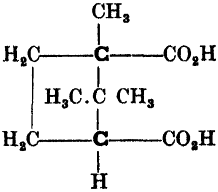
The camphor molecule is not symmetrical, and it contains two centres of asymmetry, shown in clarendon type in formula (IV) below. Nevertheless, the ketone can only exist in one *d*-, one *l*-, and one *dl*-form, since its bicyclic nature necessitates the *cis*-arrangement of the —CO - CH_2 – bridge shown in the skeleton formula (XXXV); a *trans*- disposition of this bridge would involve a degree of strain incompatible with a stable structure.‖ When, however, this portion of the ring system is broken, as in the formation of camphoric acid (V), the full number of isomerides may be encountered (see p. 479). According to Fredga and Miettinen,¶ who have related the steric configurations of a



(IV)



(XXXV)



(V)

---

* Meisenheimer and Theilacker, *Annalen*, 1932, **493**, 33.

† Morani, *Gazzetta*, 1928, **58**, 404.

‡ Compare, *inter al.*, Landolt, *Annalen*, 1877, **189**, 333.

§ Poe and Plein, *J. Phys. Chem.* 1934, **38**, 883.

‖ Compare Aschan, *Annalen*, 1901, **316**, 212; Huckel, *ibid.* 1927, **455**, 123.

¶ *Acta Chem. Scand.* 1947, **1**, 371.

number of terpenes to that of *d*-glyceraldehyde, the bridge in *d*-camphor, *d*-α-pinene and *d*-fenchone, as normally written, lies behind the plane of the paper.

The resolution of *dl*-camphor into its enantiomorphs has been described by Woodward, Kohman and Harris[*] who separated, by fractional crystallisation, l-*camphor*-l-*menthydrazone* (m.p. 193–194°, $[\alpha]_D^{25^\circ} - 58^\circ$, in alcohol) and d-*camphor*-l-*menthydrazone* (m.p. 177–178°, $[\alpha]_D^{25^\circ} - 135{\cdot}5^\circ$, in alcohol).

Camphor and its derivatives have been extensively used in investigations into the effect of structure on optical rotatory power, more especially by Lowry, Rupe, Tschugaev, and their collaborators.

The absorption spectrum and rotatory dispersion of camphor have been studied by numerous investigators;[†] it shows the same general absorption as other ketones, such as acetone, menthone and fenchone. Many camphor derivatives have also been examined in the same way.[‡] The heat of combustion has been determined by a number of investigators, including Roth and Östling,[§] who obtained the value, 1412·7 kg.-cals. The very high freezing-point depression constant, *K* 400°, which is shown by camphor, has led to its use as a solvent in molecular weight determinations, an extremely simple and accurate method having been devised by Rast.[‖]

Camphor is sparingly soluble in water, but readily so in the majority of organic solvents, in concentrated sulphuric acid[¶] and in liquid sulphur dioxide.[**] When fragments of camphor are thrown on to water, the changes in surface tension cause them to move about rapidly on the surface. Camphor is of great technical importance, and is used largely in the manufacture of celluloid, smokeless powders, explosives and for medicinal purposes; and, in addition to being obtained from natural sources, it is now manufactured on a considerable scale from pinene. The so-called "synthetic" camphor is as a rule optically inactive, although it is possible by using pinene of high rotatory power to obtain either *d*- or *l*-camphor in an optically pure state. For the manufacture of camphor there are two general processes, both of which start from bornyl chloride. In the first [scheme (*a*)] the bornyl chloride is converted into camphene by the removal of hydrogen chloride and this is then oxidised to camphor. In the second [scheme (*b*)] the camphene is hydrated to *iso*borneol, which is then oxidised catalytically to the ketone.

---

[*] *J. Amer. C.S.* 1941, **63**, 120.

[†] *Inter al.*, Baly, Marsden and Stewart, *J.C.S.* 1906, **89**, 980; Hartley, *ibid.* 1908, **93**, 963; Lowry and Desch, *ibid.* 1909, **95**, 815; Hantzsch, *Ber.* 1912, **45**, 553; Henderson, Henderson and Heilbron, *ibid.* 1914, **47**, 881; Patterson, Dunn, Buchanan and Loudon, *J.C.S.* 1932, p. 1715. For the Raman spectrum of camphor, see Jatkar and Padmanabhan, *Ind. J. Phys.* 1936, **10**, 55.

[‡] *Inter al.*, Lowry *et al. J.C.S.* 1924, **125**, 1921; 1926, p. 606; 1937, p. 233; Mathieu and Perrichet, *Compt. rend.* 1935, **200**, 1583; Singh and Prasad, *Proc. Ind. Acad. Sci.* 1936, **3** A, 586.

[§] *Ber.* 1913, **46**, 313.

[‖] *Ibid.* 1922, **55**, 1051; compare Le Fèvre and Tideman, *J.C.S.* 1931, p. 1729.

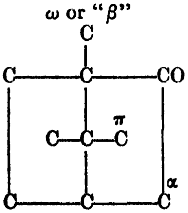
[¶] Marsh and Hartridge, *J.C.S.* 1898, **73**, 853.

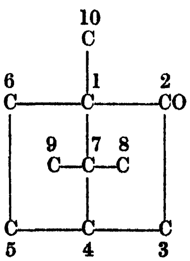
[**] Centnerszwer, *Z. Phys. Chem.* 1903, **46**, 478.

(*a*) Pinene → Bornyl chloride → Camphene → Camphor.
(*b*) Pinene → Bornyl chloride → Camphene → *iso*Borneol → Camphor.

The latter method, although it involves an extra stage, is the one most generally adopted, since it has been found to be the more economic. Consideration of the details of the various reactions lies outside the scope of this book, but several excellent accounts have been written.*

Before proceeding to discuss the properties of camphor it is necessary to refer to the nomenclature used in describing its substitution products. Substituting groups take up three positions, which, in the older literature, are always designated α, β and π; more recently, numerals have been used. Furthermore, since it has been shown that the so-called "β"-substitution products are 10- and not 6-derivatives, they are more correctly described by the use of the prefix ω-, and this convention has been adopted in the sequel.



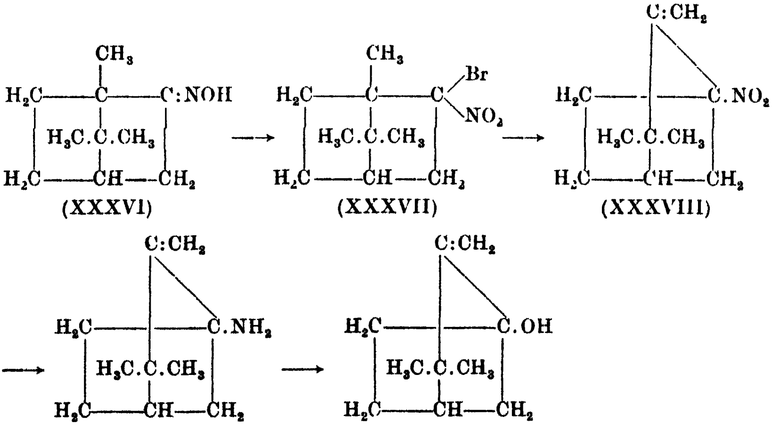


---

* Aschan, *Die Naphtenverbindungen, Terpene und Campherarten*, pp. 163–173; Brus, *Bull. Inst. Pin*, 1934, p. 100; 1936, pp. 8, 57, 73; Gubelmann and Elley, *Ind. Eng. Chem.* 1934, **26**, 589. See also *Thorpe's Dictionary of Applied Chemistry*, 4th ed. Vol. II, p. 249. London, 1938.

It will be obvious that α corresponds to 3, ω to 10 and π to 8 or 9. The two hydrogen atoms attached to the α-carbon atom are not stereochemically equivalent, so that two isomeric α-substitution products can theoretically exist and have actually been prepared. The same holds true in the case of certain other substitution products; two stereoisomeric π-hydroxycamphors, for example, have been obtained. It will be convenient to discuss here the debated question of the constitution of the "β"-substitution products. The actual position of the substituting group has, in this case, been the subject of considerable discussion and until comparatively recently the general consensus of opinion* was that it was attached to carbon atom 6, but evidence has now been adduced which shows conclusively that the "β"-substitution actually occurs at carbon atom 10, i.e. in the ω-position.

In 1902 Forster prepared a new *bromocamphor*, m.p. 78°, $[\alpha]_D$ + 19° (in alcohol). This substance was obtained by the action of bromine on 1-hydroxycamphene, which had itself been prepared by a somewhat lengthy series of operations, which need only be summarised here, since they have been discussed already on p. 313. From d-*camphoroxime* (XXXVI) *bromonitrocamphane* (XXXVII) was prepared, which gave by the action of silver nitrate a nitrocamphene (XXXVIII). This yields on reduction

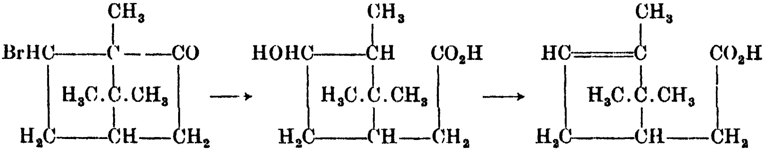


---

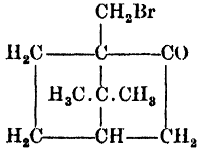
* Compare Kipping and Pope, *J.C.S.* 1895, **67**, 371; Kipping, *ibid.* 1896, **69**, 913; Forster, *ibid.* 1902, **81**, 267; Armstrong and Lowry, *ibid.* 1469.

aminocamphene (XXXIX), from which, by the action of nitrous acid, 1-hydroxycamphene (XL) is obtained.* It was from this alcohol that the new bromocamphor was prepared by the action of bromine.

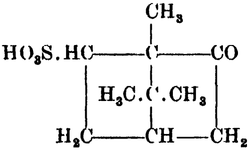
There can be no doubt that it is a true derivative of camphor, since it yields camphor on reduction with zinc dust, and α-*campholenic acid* (XLII) on treatment with alkali. This latter reaction was interpreted as an indication that the bromine atom in the bromocamphor was in position 6 (XLI). It was suggested by Forster that, if it were attached to carbon atom 10 (XLIII), this reaction would be very much less likely to take place.



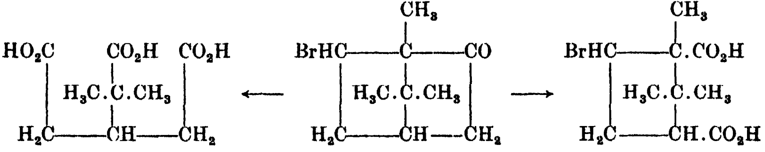
(XLI) (XLII)



(XLIII)



(XLIV)



(XLVI) (XLI) (XLV)

Simultaneously, and by an entirely different series of reactions, Armstrong and Lowry† prepared the same bromocamphor. Some years before, Reychler‡ had shown that camphor could be sulphonated in acetic anhydride solution to yield a well-defined crystalline sulphonic acid, generally known as Reychler's *camphorsulphonic acid* which he formulated as (XLIV). Armstrong and Lowry found that when the sulphonyl bromide was heated it was converted into Forster's bromocamphor.[*] On oxidation with nitric acid a bromocamphoric acid was obtained, whilst with the same reagent in the presence of silver nitrate *iso*camphoronic acid (XLVI) was formed. The isolation of the latter acid was regarded as conclusive proof that the bromocamphor must have formula (XLI) and the bromocamphoric acid (XLV).

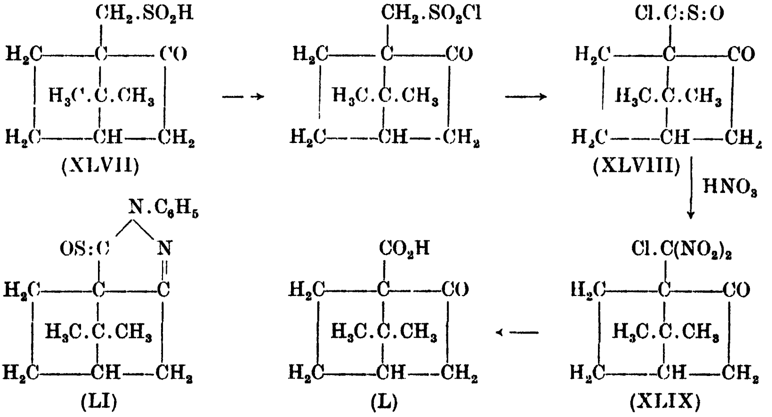
---

* Forster, *J.C.S.* 1901, **79**, 644.

† *J.C.S.* 1902, **81**, 1469.

‡ *Bull. Soc. chim.* 1898 [iii], **19**, 120.

In 1923, however, Wedekind, Schenk and Stüsser[†] showed by an elegant series of reactions that Reychler's acid actually had the sulphonic group in position 10 and that it must be represented by formula (XLVII). When the sulphochloride of the acid is treated with triethylamine or with pyridine, 10-*chlorocamphor sulphoxide*, $C_{10}H_{13}O_2ClS$, m.p. 85°, $[\alpha]_D$ −136·2°, is obtained. The constitution of this sulphoxide (XLVIII) was proved (i) by its nitration to 10:10-*dinitro*-10-*chlorocamphor* (XLIX), m.p. 150·5°, $[\alpha]_D$ −55·4°, and (ii) by the hydrolysis of this and the direct oxidation of the sulphoxide to *ketopinic acid* (L). Confirmation of the structure of the sulphoxide was obtained by a study of its reaction with phenylhydrazine, when the *pyrazolone* derivative (LI) was formed.



(XLVII) (XLVIII) (XLIX) (L) (LI)

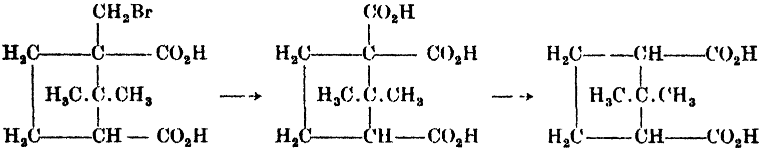
The conclusion that Reychler's acid, and also the Forster-Armstrong-Lowry "β"-bromocamphor, contained the substituent in the 10-position, still occasioned some difficulty[*] since, at that time, all attempts to convert "β"-bromocamphor into the corresponding primary alcohol had resulted in the formation of α-campholenic acid, and no reaction was known in which the bromo-ketone behaved as if it contained the grouping —CH_2Br. It is only more recently[†] that it has been found possible to achieve the conversion into 10-hydroxycamphor, the acetate of which is obtained when "β"-bromocamphor is treated with potassium acetate in acetic acid solution (see p. 432).

---

[*] The conversion of the sulphonic acid into bromocamphor has also been carried out by Loudon (*J.C.S.* 1933, p. 823), the reactions proceeding through the sulphonic acid and the mercurichloride derivatives.

[†] *Ber.* 1923, **56**, 633.

Confirmatory evidence has also been provided by Komppa,[‡] who has shown that the *bromocamphoric acid*, obtained on oxidation of "β"-bromocamphor, must have formula (LII), since replacement of the halogen by hydroxyl, followed by oxidation, gives the *carboxyapocamphoric acid* (LIII), m.p. 195–196°, which on heating is readily decarboxylated to give cis-*apocamphoric acid* (XXV). Furthermore, the bromocamphoric acid (LII) differs from the true β-bromocamphoric acid (XLV) which has been prepared indirectly by Toivonen.[§]



(LII) (LIII) (XXV)

Finally, the more recent studies of the mechanism of the sulphonation of camphor, which are discussed on p. 425, are not incompatible with the introduction of the substituent at the 10- (i.e. ω-) position. In the sequel, therefore, the "β"-derivatives, discussed above, will be given the correct prefix ω- (or 10-).

The early experiments on the reduction of camphor,[‖] involving as they did the use of acid reagents (hydriodic acid) and high temperatures, did not yield camphane but mixtures of monocyclic hydrocarbons, the exact nature of which has not been determined. The reduction to the stereoisomeric secondary alcohols, borneol and *iso*borneol, was first carried out by Berthelot* by the action of an alcoholic solution of potassium hydroxide, a reaction which can be more readily effected by sodium in a neutral solvent† (see p. 350). More recently the catalytic hydrogenation of camphor has been studied. Although camphor cannot be reduced readily by the Sabatier-Senderens process,‡ Ipatiev§ has shown that in the presence of nickel oxide at 320-350° hydrogenation does occur if high pressure is used, a mixture of borneol and *iso*borneol being obtained. If, however, a catalyst consisting of a mixture of nickel oxide and alumina is employed, then *iso*camphane is formed. There would appear to be no doubt (compare p. 276) that in this latter reaction the alcohols which are first formed undergo dehydration to camphene, which is then reduced. Vavon and Peignier‖ have found that, although the reaction proceeds somewhat slowly, camphor can be hydrogenated at the ordinary temperature in the presence of platinum black. Very little borneol is formed, *iso*borneol being the main product. If the hydrogenation is prolonged, complete reduction to camphane takes place. By the reduction of camphor with sodium in moist ethereal solution Beckmann¶ obtained, in addition to *iso*borneol and borneol, a *pinacone*, m.p. 157-158°, $[\alpha]_D$ −27·2°, which he represented by (LIV).

---

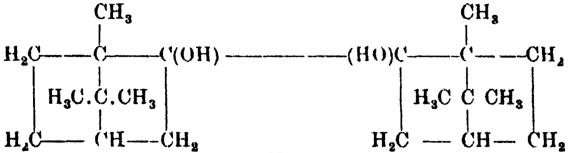
[*] See *inter al.*, Lipp and Lausberg, *Annalen*, 1924, **436**, 274; Burgess and Lowry, *J.C.S.* 1925, **127**, 279.

[†] Iki, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1934, **25**, 78.

[‡] *J. pr. Chem.* 1943 [ii], **162**, 19.

[§] *Annal. Acad. Sci. Fennicae*, 1927, A, **29**, no. 10.

[‖] Weyl, *Ber.* 1868, **1**, 94; Berthelot, *Bull. Soc. chim.* 1869 [ii], **11**, 98; Markownikov, *Ber.* 1897, **30**, 1216.



(LIV)

Being a saturated dicyclic ketone, camphor is comparatively resistant to the action of oxidising agents. It is probable that, in alkaline solution at any rate, it is the enolic form of the ketone (LV) which undergoes oxidation, *camphorquinone* (LVI) being an intermediate stage in its oxidation to camphoric acid. The further products of the oxidation are as a rule degradation products of this acid, which, in view of its importance, is discussed in detail later (p. 478).

---

* *Annalen*, 1859, **110**, 368.

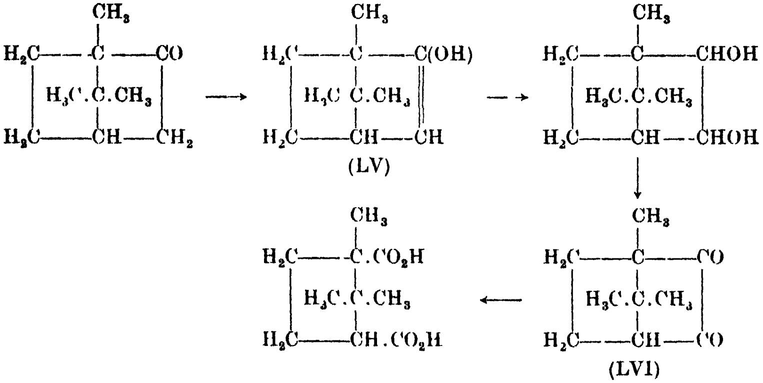
† Baubigny, *Compt. rend.* 1866, **63**, 221.

‡ Compare, however, *G.P.* 213154.

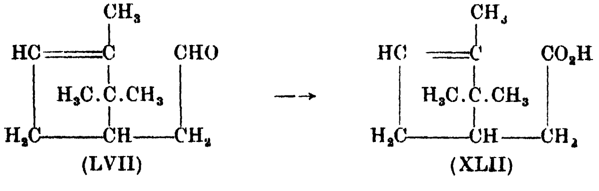
§ *Ber.* 1912, **45**, 3206.

‖ *Compt. rend.* 1925, **181**, 184; compare Lipp, Oeckinghaus and Conze, *Ber.* 1941, **74**, 6.

¶ *Ber.* 1889, **22**, 912; 1894, **27**, 2348; *J. pr. Chem.* 1897 [ii], **55**, 35; *Annalen*, 1896, **292**, 1.



Oxidation in dilute alcoholic solution in the presence of sunlight was found by Ciamician and Silber* to give a complex mixture of substances, from which they separated *α-campholenaldehyde* (LVII), identified by oxidation to α-campholenic acid (XLII) and an unsaturated *ketone*, $C_{10}H_{16}O$, b.p. 203-204°, *semicarbazone*, m.p. 151–152°. The constitution of this ketone was not determined.



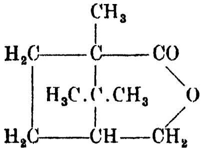
By the action of Caro's reagent Baeyer and Villiger† obtained a mixture of *α-campholide* (XIII) and a *lactone*, $C_{10}H_{16}O_4$, m.p. 189–191°. The constitution of this lactone has not been determined, but Locquin‡ has shown that when it is warmed with dilute sulphuric acid it yields a ketone, $C_9H_{14}O$, b.p. 82–86°/10 mm., $d_{0^{\circ}}^{4^{\circ}}$ 1·062, semicarbazones, m.p. 198° and 150°. This ketone must be 1:1:2:5-*tetramethyl*-Δ^4-cyclo*penten*-3-*one* (LVIII), since it gives on oxidation with potassium permanganate *γ-keto-αββ-trimethylvaleric acid* (LIX), which was identified by its oxidation with sodium hypobromite to *trimethylsuccinic acid* (XIX).

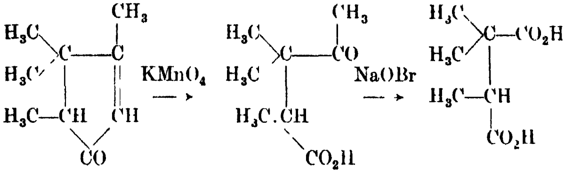
---

* *Ber.* 1910, **43**, 1341.

† *Ibid.* 1899, **32**, 3625.

‡ *Compt. rend.* 1911, **153**, 284.

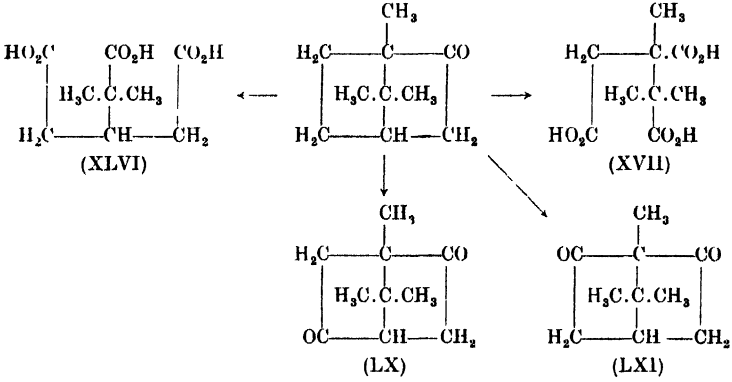

(XIII)



(LVIII) (LIX) (XIX)

Camphor is smoothly converted in excellent yield into camphorquinone by oxidation with selenium dioxide.*

Kachler† found that camphor was only very slowly attacked by chromic acid, but on prolonged warming a mixture consisting essentially of *camphoronic acid* (XVII) and iso*camphoronic acid* (XLVI) was obtained. Both these acids have been prepared synthetically, the former by Perkin and Thorpe‡ and by Ganguly,§ and the latter by Perkin.‖


(XLVI) (XVII) (LX) (LXI)

Subsequently, Bredt¶ showed that if the oxidation is carried out in acetic acid solution in the absence of mineral acids p-*diketocamphane* (LX) is obtained. According to Miyake and Watanabe[*] some 6-*ketocamphor* (LXI), m.p. 195°, is also formed. The oxidation proceeds therefore in an analogous manner to that of bornyl acetate (p. 361). Potassium permanganate does not attack camphor in neutral solution, but in alkaline solution camphoric acid is obtained,[†] the same acid being formed also by the action of potassium ferricyanide.[‡] As has been mentioned on p. 374, it was observed many years ago that camphor was oxidised by concentrated nitric acid to camphoric acid; the products of this oxidation have been the subject of repeated study[§] and, in addition to camphoric acid, camphoronic, *iso*camphoronic, trimethylsuccinic and dimethylsuccinic acids have been found to be formed. A remarkable oxidation product, benzene pentacarboxylic acid, was stated by Schrötter and Weitzenbock[‖] to result when camphor is first treated with concentrated sulphuric acid in the presence of mercury and then warmed with nitric acid. Since the acid contains eleven carbon atoms it is obvious that condensation, accompanied by molecular rearrangement, must precede the oxidation, but the mechanism of the reaction is obscure.

---

* Evans, Ridgion and Simonsen, *J.C.S.* 1934, p. 137; compare Vène, *Compt. rend.* 1943, 216, 772.

† *Ber.* 1880, **13**, 487.

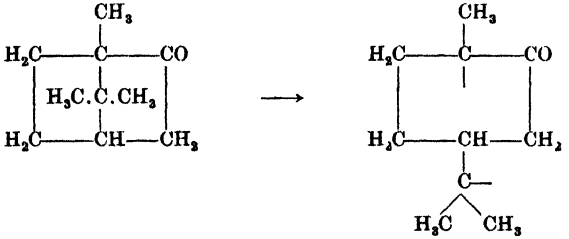
‡ *J.C.S.* 1897, **71**, 1169.

§ *J. Ind. C.S.* 1943, **20**, 101.

‖ *J.C.S.* 1902, **81**, 246.

¶ *J. pr. Chem.* 1923 [ii], **106**, 336.

By the action of dehydrating agents on camphor, monocyclic substances are obtained, but since the formation of these is frequently associated with molecular rearrangement the products are of little value in elucidating the constitution of the parent ketone. As a rule, ring fission occurs between the 1 and 7 carbon atoms leading primarily to derivatives of *p*-cymene:



---

[*] *Proc. Imp. Acad. Tokyo*, 1935, **11**, 106.

[†] Grosser, *Ber.* 1881, **14**, 2507.

[‡] Étard, *Compt. rend.* 1900, **130**, 570.

[§] *Inter al.*, Kachler, *Annalen*, 1871, **159**, 286; 1878, **191**, 148; *Ber.* 1880, **13**, 487; Kullhem, *Annalen*, 1872, **163**, 232; Roser, *Ber.* 1885, **18**, 3112; Bredt, *ibid.* 1893, **26**, 3047.

[‖] *Monatsh.* 1908, **29**, 396 749.

The formation of *p*-cymene (Kamfogene) from camphor was apparently first observed by Dumas and Péligot,[*] who treated the ketone with phosphorus pentoxide, its identity being later confirmed by Kekule and Pott[†] and by Armstrong and Miller.[‡] With zinc chloride the dehydration proceeds in a very complex manner, Armstrong and Miller showing that *p*-cymene, 1:2-dimethyl-4-ethylbenzene, 1:2:3:5-tetramethylbenzene and carvacrol were formed. It had, however, been observed much earlier by Claus[§] that carvacrol could be obtained from camphor by heating it with iodine, although the identity of the phenol was only established much later by Fleischer and Kekule.[‖] Of greater interest were the results obtained on treatment of the ketone with sulphuric acid. The early experiments of Delalande,[¶] Chataud,[**] Schwanert[††] and Kachler[‡‡] had shown that when the ketone was heated with concentrated sulphuric acid an oxygenated body was formed to which the name camphrene was given. This was subsequently found by Armstrong and Kipping[§§] and by Bredt, Rochussen and Mohnheim[‖‖] to consist essentially of a mixture of 3:4-dimethylacetophenone and carvenone (Vol. I, p. 345).

THE HALOGEN DERIVATIVES OF CAMPHOR

By the direct halogenation of camphor, substitution of the hydrogen atom attached to the α- (or 3-) carbon atom occurs readily with the formation of monohalogenated derivatives. Such substituted camphors should exist in two stereoisomeric modifications which may be represented by formulae (I) and (I a), where R = Cl or Br, and it is further obvious that disubstitution products with different substituents attached to this carbon atom should exist also in two modifications, (II) and (IIa). Owing mainly to the ingenious experiments of Lowry and his collaborators many of these isomerides have been prepared and their reactions investigated.

---

[*] *Compt. rend.* 1836, **4**, 496.

[†] *Ber.* 1869, **2**, 121.

[‡] *Ibid.* 1883, **16**, 2259.

[§] *Annalen*, 1842, **44**, 301; *J. pr. Chem.* 1843, **25**, 264.

[‖] *Ber.* 1873, **6**, 935; compare Armstrong and Easkill, *ibid.* 1878, **11**, 151; Armstrong and Miller, *ibid.* 1883, **16**, 2255.

[¶] *Compt. rend.* 1839, **9**, 608.

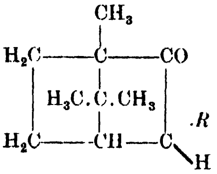
[**] *Ibid.* 1857, **44**, 66.

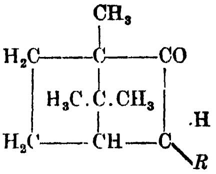
[††] *Annalen*, 1862, **123**, 298.

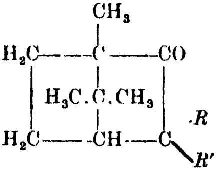
[‡‡] *Ibid.* 1872, **164**, 80.

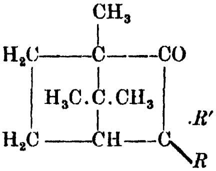
[§§] *J.C.S.* 1893, **63**, 75.

[‖‖] *Annalen*, 1900, **314**, 376.

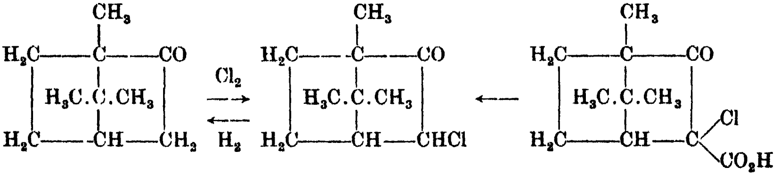

(I)


(Ia)


(II)


(IIa)

By the chlorination of camphor in alcoholic solution Cazeneuve* prepared a *chlorocamphor*, m.p. 92–95°, $[\alpha]_D$ +90° (in alcoholic solution), the same substance being obtained also by Schiff and Puliti† and by Balbiano‡ by heating *chlorocamphorcarboxylic acid* (III). Since this chlorocamphor gives on reduction camphor, and on oxidation with potassium permanganate camphoric acid, it must be represented by formula (IV), substitution having taken place at the α- (3-) carbon atom.


(IV) (III)

Both Cazeneuve and Balbiano obtained evidence of the presence of an isomeric monochlorocamphor having a higher melting-point and a different rotatory power, but this substance was first prepared in a pure state by Lowry and Steele.* Kipping† had made the interesting observation that alcoholic solutions of both α-chloro- and α-bromocamphors showed mutarotation when alkali was added. This change in rotatory power was due to the formation of an equilibrium mixture of the two stereoisomeric modifications of the monosubstituted halogen derivatives, α- and α′-monochlorocamphors. By a prolonged fractional crystallisation of an alcoholic solution of α-chlorocamphor, which had been isomerised by the addition of a trace of sodium ethoxide, Lowry and Steele succeeded in separating the more soluble α′-chlorocamphor.

---

* *Bull. Soc. chim.* 1882 [ii], **37**, 454; **38**, 9; 1883 [ii], **39**, 116, 501.

† *Ber.* 1883, **16**, 888.

‡ *Gazzetta*, 1887, **17**, 96, 243.

α-Chlorocamphor has m.p. 94°, $[\alpha]_D$ +96·2° (in alcohol, $c = 5$), whilst the very much more readily soluble *α′-chlorocamphor* melts at 117°, $[\alpha]_D$ +35° (in alcohol, $c = 5$). The latter is somewhat unstable and on keeping tends to lose hydrogen chloride. If, to a concentrated alcoholic solution of α′-chlorocamphor, a drop of sodium ethoxide be added, isomerisation occurs, and the more sparingly soluble α-chlorocamphor crystallises from the equilibrium mixture. In dilute solution the change can be followed by observing the mutarotation. The following figures quoted from Lowry and Steele's memoir will serve to make this clear:

	α_{5461} Without alkali	α_{5461} After addition of alkali
α-Chlorocamphor	+2·42°	+2·29°
α′-Chlorocamphor	+0·92°	+2·28°

Results of considerable interest have accrued from a study of the bromination of the two chlorocamphors. By the action of bromine on α-chlorocamphor (V) Lowry‡ obtained an isomorphous mixture of two chlorobromocamphors and the same mixture was obtained by the chlorination of α-bromocamphor (VI) (p. 400). The two isomerides, *α′-chloro-α-bromocamphor* (VII), $[\alpha]_D$ +64°, and *α-chloro-α′-bromocamphor* (VIII), $[\alpha]_D$ +10°, were not obtained quite pure.

The same mixture of isomerides was obtained by the bromination of α′-chlorocamphor (IX) and this result supports

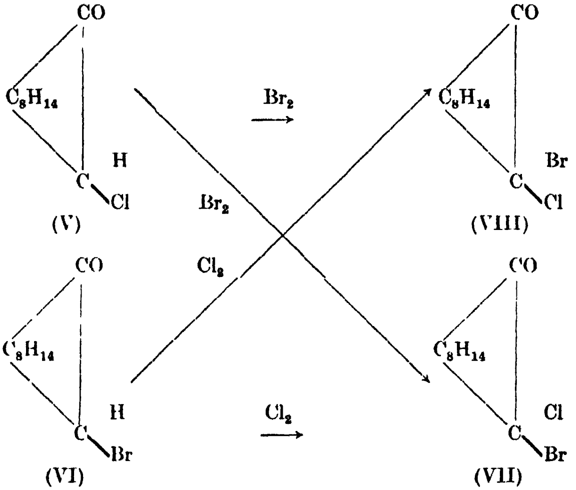
---

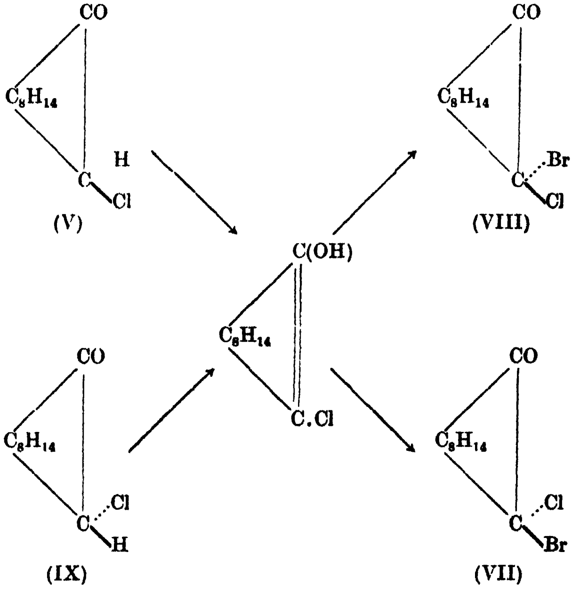
* *J.C.S.* 1915, **107**, 1382.

† *Proc. C.S.* 1905, **21**, 124.

‡ *J.C.S.* 1898, **73**, 569.

Lapworth's theory,* that the halogenation in this and in other analogous cases proceeds through the enolic form.





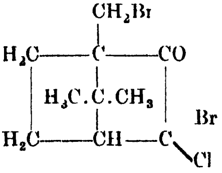
---

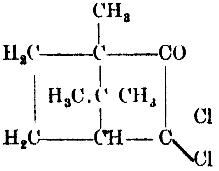
* *J.C.S.* 1904, 85, 30.

On the other hand, the nitration of α-chlorocamphor and α′-chlorocamphor appears to proceed in a more simple manner. Thus α-chlorocamphor yields *α-chloro-α′-nitrocamphor*, whilst α′-chlorocamphor gives *α′-chloro-α-nitrocamphor*, the chlorination of α-nitrocamphor (p. 410) giving α′-chloro-α-nitrocamphor. The properties of these derivatives are shown in the following table:[*]

	M.p.	$[\alpha]_D$ (in chloroform)
α-Chloro-α′-nitrocamphor	95°	− 5°
α′-Chloro-α-nitrocamphor	132°	+ 13°

When α-chlorocamphor is heated with an excess of bromine in a sealed tube a mixture of chlorobromocamphors is obtained from which Lowry[†] succeeded in separating a homogeneous *chlorodibromocamphor*, m.p. 84°, $[\alpha]_D$ + 51·2°. It seems probable that this substance is *α-chloro-α′ω-dibromocamphor* (X), but the position of the bromine atoms has not been definitely established.

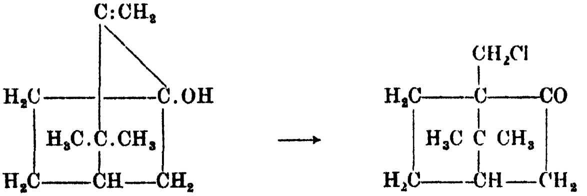

(X)


(XI)

Neither α- nor α′-chlorocamphor yields oximes, but give, like α-bromocamphor, on treatment with hydroxylamine a mixture of isomeric camphorquinonedioximes (p. 477).[‡]

By the saturation of an alcoholic solution of camphor with chlorine, Cazeneuve[§] prepared *αα′-dichlorocamphor* (XI), m.p. 96°, $[\alpha]_D$ + 57·3°.

ω- (or 10-) *Chlorocamphor* (XIII) was prepared by Forster[‖] by the action of chlorine on 1-hydroxycamphene (XII) in acetic acid


(XII) (XIII)

---

[*] Lowry, *J.C.S.* 1898, **73**, 987.

[†] *J.C.S.* 1898, **73**, 584.

[‡] Burgess, *ibid.* 1924, **125**, 2376.

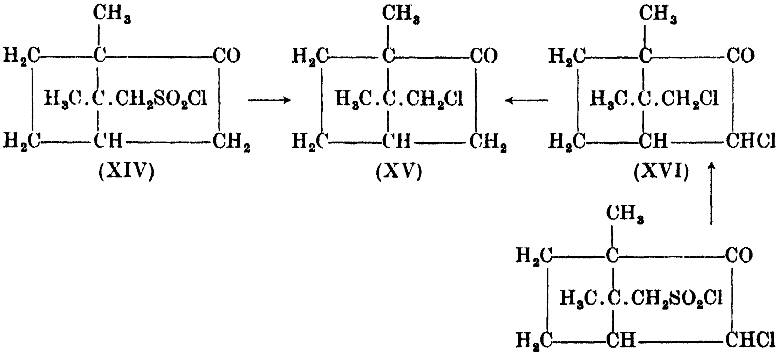
[§] *Bull. Soc. chim.* 1882 [ii], **37**, 454.

[‖] *J.C.S.* 1902, **81**, 272.

solution in the presence of sodium acetate. It is formed also by the action of hypochlorous acid on this substance.[*]

ω-Chlorocamphor, the constitution of which has been discussed on p. 386, has m.p. 132·5°, $[\alpha]_D$ +40·7° (in alcohol). It gives an *oxime*, m.p. 101°, $[\alpha]_D$ +126·5° (in chloroform).

π- (or 8-) *Chlorocamphor*[†] (XV), m.p. 139–139·5°, $[\alpha]_D$ +99·88° (in chloroform), was prepared by Kipping and Pope[‡] by heating *camphor-π-sulphonyl chloride* (XIV) (p. 422) at 175–190°. It is formed also when *απ-dichlorocamphor* (XVI), m.p. 118–118·5°, $[\alpha]_D$ + 96·74° (in chloroform), is reduced with sodium amalgam in alcoholic solution. The latter can be prepared by heating *α-chloro-camphor-π-sulphonyl chloride* (XVII) at 160–180°.



(XIV) (XV) (XVI) (XVII)

The bromination of camphor proceeds with great facility and *α-bromocamphor* (XVIII) has been prepared by a number of reactions. When camphor is mixed with bromine an unstable red crystalline additive compound, $C_{10}H_{16}O, Br_2$, is formed,[§] which is best prepared by the addition of bromine to a chloroform solution of the ketone.[‖] This compound, when gently warmed, decomposes with the evolution of hydrogen bromide and formation of α-bromocamphor.[¶] The bromide can, however, be prepared more conveniently by the slow addition of bromine to camphor heated on the water bath,[*] or by the addition of bromine to an alcoholic solution of the ketone.[†] Indirectly, α-bromocamphor has been obtained by the action of bromine on *hydroxymethylenecamphor* (XIX),[‡] by heating *α-bromocamphorcarboxylic acid* (XX)[§] and by the action of alcoholic potassium hydroxide on this acid.[||]

---

[*] Forster and Howard, *ibid.* 1913, **103**, 63.

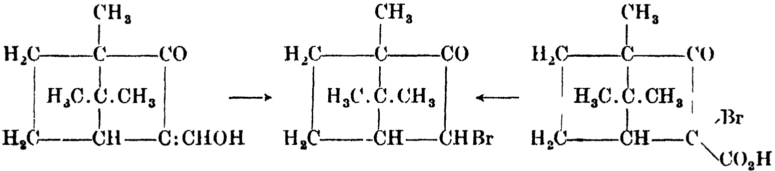
[†] Since the two methyl groups, 8- and 9-, are not identical, they should on substitution yield different chlorocamphors, but these have not been described.

[‡] *J.C.S.* 1895, **67**, 377.

[§] Laurent, *Compt. rend.* 1840, **10**, 532; *Annalen*, 1844, **48**, 251.

[‖] Swarts, *Jahresbericht*, 1862, p. 462; Perkin, *J.C.S.* 1865, **18**, 92.

[¶] Keller, *Chem. Z.* 1880, **4**, 156.



(XIX) (XVIII) (XX)

d-α-Bromocamphor has m.p. 76–77° (*dl*-, m.p. 51·1°), $[\alpha]_D$ + 117·1° (in benzene, $c = 1{\cdot}6$); the optical rotatory power shows very marked variations depending upon the solvent and the concentration. The constitution of the bromide is proved by its oxidation with potassium permanganate to camphoric acid;[¶] on reduction with sodium amalgam in alcoholic solution camphor is obtained.[**]

The reactions of the bromide have been studied in great detail and it will only be possible to refer here to the more important of these. As mentioned already, it yields with chlorine a mixture of the two isomeric chlorobromocamphors, whilst when brominated at 100° *αα′-dibromocamphor* (p. 405) is obtained.[††] If, however, it be heated at 110–120° with one and a half mols. of bromine, αω-dibromocamphor (p. 407) is formed.[‡‡] When α-bromocamphor (XXI) is warmed with nitric acid it yields a mixture of camphoric acid, *α-bromo-α′-nitrocamphor* (XXII) and αα′-dibromocamphor.[§§] The latter substance owes its formation to the bromination of α-bromocamphor by the bromine liberated during the oxidation of a portion of the bromide to camphoric acid. α-Bromo-α′-nitrocamphor has m.p. 107°, $[\alpha]_D$ $-22°$ (in chloroform, $c = 10$), the isomeric *α′-bromo-α-nitrocamphor* (XXIII), m.p. 106°, $[\alpha]_D$ $+53°$ (in chloroform, $c = 0{\cdot}5$) being obtained when *α′-nitrocamphor* (XXIV) is brominated;[*] in this bromination α-bromo-α′-nitrocamphor is also formed. When α-bromo-α′-nitrocamphor is reduced it yields α′-nitrocamphor.[†]

---

[*] Armstrong and Matthews, *Chem. News*, 1878, **37**, 4; Kipping and Pope, *J.C.S.* 1893, **63**, 576; compare Ingersoll and Babcock, *J. Amer. C.S.* 1933, **55**, 341.

[†] Marsh, *J.C.S.* 1890, **57**, 828.

[‡] Claisen, Bishop and Sinclair, *Annalen*, 1894, **281**, 345.

[§] de Santos e Silva, *Ber.* 1873, **6**, 1093.

[||] Aschan, *Ber.* 1894, **27**, 1445.

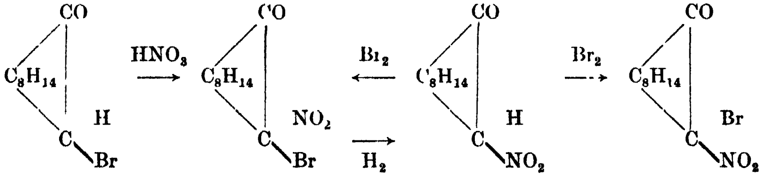
[¶] Balbiano, *Gazzetta*, 1887, **17**, 242.

[**] Montgolfier, *Ann. Chim.* 1878 [v], **14**, 110.

[††] Schiff, *Ber.* 1880, **13**, 1402; Cazeneuve, *Bull. Soc. chim.* 1884 [ii], **42**, 69; Lowry, *J.C.S.* 1898, **73**, 988.

[‡‡] Kachler and Spitzer, *Monatsh.* 1863, **4**, 486.

[§§] Schiff, *Ber.* 1880, **13**, 1402; Cazeneuve, *Bull. Soc. chim.* 1884 [ii], **42**, 69; Lowry, *J.C.S.* 1898, **73**, 988.



(XXI) (XXII) (XXIV) (XXIII)

The action of oleum on α-bromocamphor has been shown by Kipping and Pope[‡] to result in the formation of α-bromocamphor-π-sulphonic acid (p. 424), the same product being formed also by the action of chlorosulphonic acid.[§] With sodium in neutral solution, bimolecular compounds are formed, which have been studied by Oddo,[||] whilst Malmgren[¶] has shown magnesium to react in a similar manner. When treated with carbon dioxide in the presence of sodamide in ethereal solution, α-bromocamphor yields camphor-3-carboxylic acid[**] (p. 440). Goldschmidt and Korev[††] obtained camphoroxime by the action of free hydroxylamine on α-bromocamphor, but if the bromide is heated with a mixture of hydroxylamine hydrochloride and sodium acetate a mixture of camphorquinone-α- and β-dioximes (p. 471) is obtained.[‡‡] It is of interest to note that Clarke, Lapworth and Wechsler[§§] obtained *iso*nitrosocamphor by treating α-bromocamphor with *iso*amyl nitrite in the presence of sodium ethoxide.

---

[*] Lowry, *J.C.S.* 1898, **73**, 989.

[†] Schiff, *Ber.* 1876, **13**, 1403; Cazeneuve, *Bull. Soc. chim.* 1887 [ii], **47**, 920; Lowry, *J.C.S.* 1893, **73**, 991.

[‡] *J.C.S.* 1893, **63**, 577.

[§] Kipping and Pope, *ibid.* 1895, **67**, 356.

[||] *Gazzetta*, 1893, **23**, II, 316; 1897, **27**, I, 149; 1905, **35**, I, 12.

[¶] *Ber.* 1903, **36**, 2627.

[**] Bruhl, *ibid.* 1903, **36**, 1307.

[††] *Ber.* 1885, **18**, 1635.

[‡‡] Angelico and Montalbano, *Gazzetta*, **30**, II, 300; compare Burgess, *J.C.S.* 1924, **125**, 2375.

[§§] *J.C.S.* 1908, **93**, 40..

Although camphor on bromination gives an almost theoretical yield of α-bromocamphor, it has long been known that the initial product consists of a mixture of the α- and α′-isomerides. Marsh* was able to separate from the crude bromination product a fraction having a very much lower optical rotatory power, $[\alpha]_D$ +29·4°, as compared with +135° of pure α-bromocamphor, and he observed also that conversion of the former into the latter could be effected by distillation at the ordinary pressure. This method of purification is, however, much less satisfactory than that originally suggested by Armstrong,† in which crude α-bromocamphor is treated with an alcoholic solution of potassium hydroxide. So effective is this method that it was generally supposed that the reaction was irreversible. In 1905, however, Kipping‡ showed that, if alkali was added to an alcoholic solution of α-bromocamphor, the rotatory power of the solution diminished, and by working alternatively with alkaline and acid solutions he succeeded in preparing a bromocamphor having a rotatory power of the same order as that obtained by Marsh by the direct bromination of camphor. By the aid of solubility experiments, Lowry§ confirmed the presence of the second isomeride in solutions which had been treated with alkali, but it remained for Lowry, Steele and Burgess‖ to prepare pure α′-bromocamphor. This was obtained in exactly the same manner as that used for the preparation of α′-chlorocamphor, but, owing to the greater solubility of the bromide, the isolation was more difficult. *α′-Bromocamphor* crystallises from alcohol in needles, m.p. 78°, $[\alpha]_{5461}$ −40° (in alcohol, $c = 10$). If a drop of alkali be added to its alcoholic solution, the rotatory power rises owing to the formation of the α-isomeride and the solution in equilibrium contains 92 per cent. of this isomeride. The extent of the mutarotation is shown by the following values:

	$[\alpha]_{5461}$ Initial value	$[\alpha]_{5461}$ Final value (after addition of $N/1000$ $NaOC_2H_5$)
α Bromocamphor	+164·75°	+147·4°
α′-Bromocamphor	− 38·8°	+147·7°

---

* *J.C.S.* 1891, **59**, 969.

† *Chem. News*, 1878, **37**, 4.

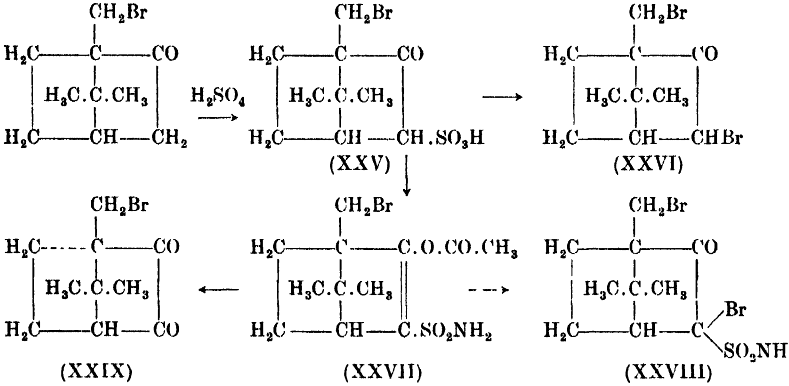
‡ *Proc. C.S.* 1905, **21**, 125.

§ *J.C.S.* 1906, **89**, 1033.

‖ *Ibid.* 1922, **121**, 633.

On nitration, α- and α′-bromocamphor, unlike α- and α′-chlorocamphors, give the same *α-bromo-α′-nitrocamphor*, m.p. 104°, $[\alpha]_D$ −27° (in alcohol).

Reference has been made on p. 387 to the preparation of ω- (or 10-) *bromocamphor*, and the constitution of this substance has also been discussed. ω-Bromocamphor crystallises in prisms, m.p. 78°, $[\alpha]_D$ +19·1° (in alcohol). Its absorption spectrum has been studied by Lowry and Desch.[*] It can be readily characterised by the preparation of the *oxime*, m.p. 156°. When treated with bromine it yields αω-dibromocamphor. On oxidation with nitric acid, in addition to ω-bromocamphoric acid, αω-dibromo-α′-nitrocamphor is also formed. Other important reactions of this dibromide are discussed on p. 407. By the sulphonation of ω-bromocamphor, Burgess and Lowry[†] prepared a bromocamphorsulphonic acid, which must be *ω-bromocamphor-α-sulphonic acid* (XXV), since when the sulphonylbromide is refluxed in xylene solution it yields a mixture of αω- and α′ω-*dibromocamphors* (XXVI). The sulphonic acid was characterised by the preparation of the *sulphonyl chloride*, m.p. 97°, and the *amide*, m.p. 100–102°, $[\alpha]_{5461}$ +46·1°. The carbonyl group in the amide shows the interesting property of reacting in the enolic form, since on digestion with acetic anhydride the *acetyl* derivative (XXVII) is obtained. On bromination this acetyl derivative gives, in addition to *α′ω-dibromocamphor-α-sulphonamide* (XXVIII), a small quantity of *ω-bromocamphorquinone* (XXIX).

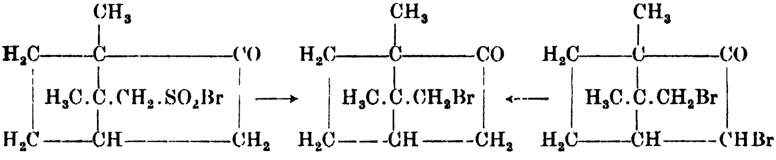


---

[*] *J.C.S.* 1909, **95**, 816.

[†] *Ibid.* 1925, **127**, 271.

π- (or 8-) *Bromocamphor* (XXX) was prepared by Kipping and Pope[*] by heating *camphor-π-sulphonyl bromide* (XXXI) at 150° or by the reduction of *απ-dibromocamphor* (XXXII) with sodium amalgam.[†] π-Bromocamphor is dimorphic, the stable form, m.p. 93·4°, crystallising from light petroleum in tetragonal prisms, whilst the labile has m.p. 60–63°, $[\alpha]_D$ +116·01°. It has been characterised by the preparation of the *oxime*, m.p. 124·5°.



(XXXI) (XXX) (XXXII)

αα'-Dibromocamphor, which was first described by Swarts,[‡] is readily obtained when α-bromocamphor is warmed on the water bath with bromine.[§] It crystallises in prisms, m.p. 61°, $[\alpha]_D$ +39·2° (in alcohol). Its absorption spectrum in the ultra-violet has been studied by Lowry and Desch.[‖] The constitution of this bromide has been proved by its reduction to camphor with sodium amalgam, by the formation of hydroxymethylenecamphor by the action of sodium methoxide in benzene solution[¶] and by its conversion into camphor-3-carboxylic acid by the action of carbon dioxide in the presence of either magnesium or sodium.[**] The action of nitric acid on αα'-dibromocamphor was investigated by Forster[††] and by Lapworth and his collaborators.[‡‡] Reference has been made on p. 381 to the formation of homocamphoronic acid by the action of this reagent and to its conversion into camphononic acid. In addition, camphoric acid and α-bromo-α'-nitrocamphor are also formed. If αα'-dibromocamphor is oxidised with nitric acid in the presence of silver nitrate, then bromocamphorenic acid is obtained, an acid which results also when Forster's *dibromocampholide* (XXXIV) is reduced with zinc dust.

---

[*] *J.C.S.* 1895, **67**, 382.

[†] Revis and Kipping, *Proc. C.S.* 1896, p. 77.

[‡] *Ber.* 1882, **15**, 1623.

[§] Lowry, *J.C.S.* 1898, **73**, 587.

[‖] *J.C.S.* 1909, **95**, 818.

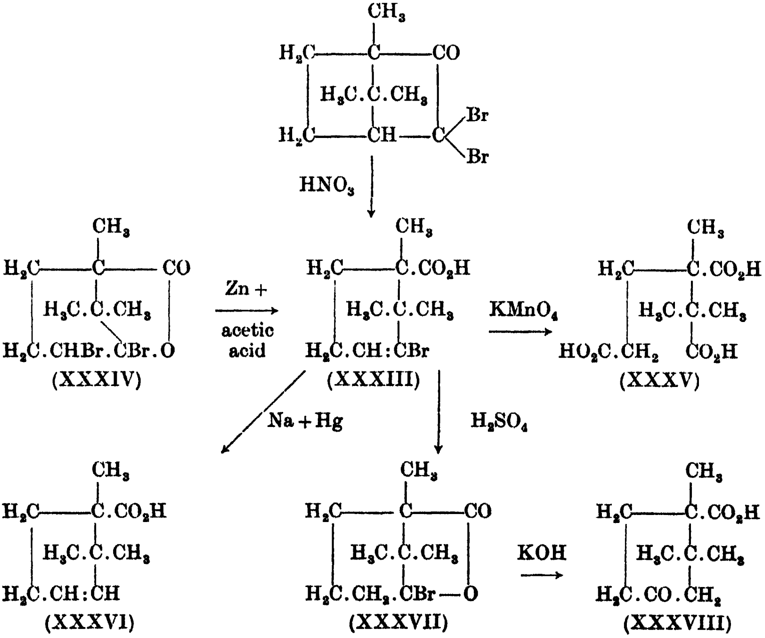
[¶] Brühl, *Ber.* 1904, **37**, 2072.

[**] Brühl, *ibid.* 1903, **36**, 4289.

[††] *J.C.S.* 1896, **69**, 36.

[‡‡] *Ibid.* 1899, **75**, 992, 1134; 1900, **77**, 311; 1902, **81**, 17.

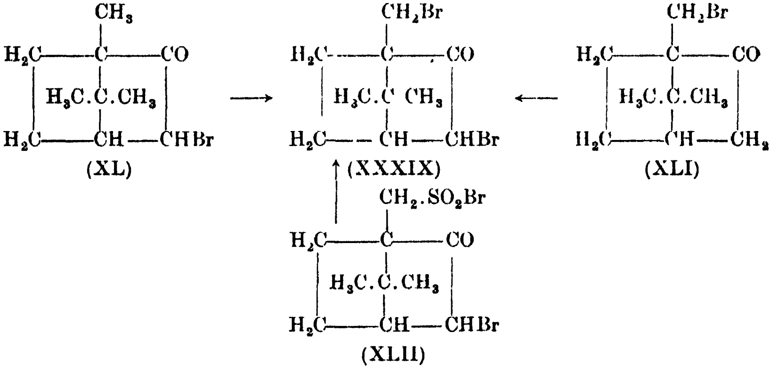
Bromocamphorenic acid, m.p. 159°, $[\alpha]_D$ +144·1°, has been shown to have the structure (XXXIII), since it gives on oxidation with potassium permanganate *homocamphoronic acid* (XXXV). When bromocamphorenic acid is reduced with sodium amalgam it yields *camphorenic acid* (XXXVI), m.p. 161°, $[\alpha]_D$ +179·4°, whilst when treated with sulphuric acid it yields *α-bromocampholide* (XXXVII), which is converted by alkali into *camphonic acid* (XXXVIII), m.p. 195°, *semicarbazone,* m.p. 222–223°. It will be observed that in the conversion of αα′-dibromocamphor into camphorenic acid a molecular rearrangement occurs. This was originally assumed (Lapworth) to proceed with the intermediate formation of a *cyclo*propane ring but, in the light of our present knowledge of the mechanism of such reactions, this assumption is no longer necessary.



αα′-Dibromocamphor is not attacked by the phosphorus halides. If it is heated in an atmosphere of hydrogen bromide at

120° under pressure it isomerises to αω-dibromocamphor,[*] whilst treatment with alkali converts it into α-bromocamphor.

Although αω- (3 : 10-) *dibromocamphor* (XXXIX) was originally prepared by Swarts[†] by heating α-bromocamphor (XL) with bromine under pressure at 110–120°, its constitution was first clearly established when Forster[‡] showed that it could be prepared by the bromination of ω-bromocamphor (XLI). At the same time Armstrong and Lowry[§] described its preparation by the action of heat on *α-bromocamphor-ω-sulphonyl bromide* (XLII).



αω-Dibromocamphor melts at 114°, $[\alpha]_{5461}$ +127° (in acetone) and it is only very slightly volatile in steam. When it is heated with concentrated nitric acid it yields *αω-dibromo-α′-nitrocamphor*, m.p. 129°, $[\alpha]_D$ −25·7°, and *αα′ω-tribromocamphor*;[‖] at the same time some oxidation occurs with the formation of ω-bromocamphoric acid. αα′ω-Tribromocamphor is obtained also when αω-dibromocamphor is warmed with bromine or with phosphorus pentabromide.[¶] When alkali is added to an alcoholic solution of αω-dibromocamphor the rotatory power falls (+99° to +81°), indicating the formation in solution of *α′ω-dibromocamphor*.[**] This isomeride has been isolated by Burgess and Lowry[††] by methods similar to those employed for the preparation of the α′-chloro- and bromo-camphors (compare p. 397). It has m.p. 136°, $[\alpha]_{5461}$ +85° (in acetone, $c = 5$). By the reduction of αω-dibromocamphor with sodium amalgam Kachler and Spitzer[*] obtained a substance which they considered to be a hydroxy-camphor, but this has since been shown to be α-campholenic acid (XLIII). When treated with sodium methoxide or ethoxide a similar degradation occurs, α-bromocampholenic acid (XLIV) being obtained.[†] These reactions, which are analogous to the conversion of ω-bromocamphor into α-campholenic acid, are illustrated by the scheme:

---

[*] Swarts, *Ber.* 1882, **15**, 2135.

[†] *Zeit. für Chem.* 1866, p. 628; *Ber.* 1882, **15**, 1622, 2135.

[‡] *J.C.S.* 1902, **81**, 270.

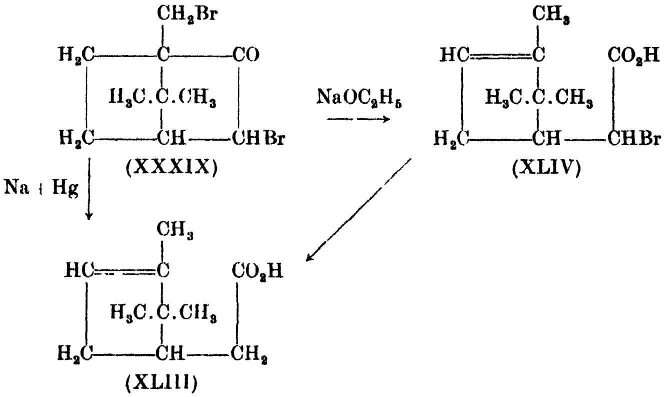
[§] *Ibid.* 1902, **81**, 1451.

[‖] Kachler and Spitzer, *Monatsh.* 1882, **3**, 218; 1883, **4**, 566; Armstrong and Lowry, *J.C.S.* 1902, **81**, 1462.

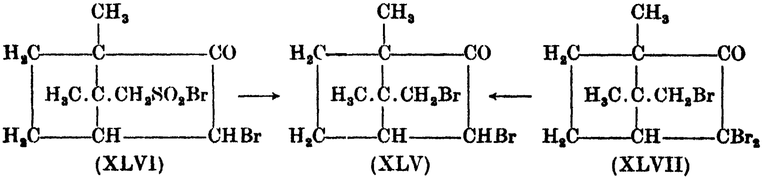
[¶] Swarts, *Ber.* 1882, **15**, 1625; de la Royère, *ibid.* p. 1621.

[**] Lowry, *J.C.S.* 1906, **89**, 1037.

[††] *J.C.S.* 1923, **123**, 1873.



απ-Dibromocamphor (XLV), m.p. 156°, $[\alpha]_D$ +128·2° (in acetone), was prepared by Kipping and Pope[‡] by heating *α-bromocamphor-π-sulphonyl bromide* (XLVI) to 165°. It has been obtained also by the action of alkali on *αα′π-tribromocamphor* (XLVII).[§] On treatment with concentrated nitric acid it yields



---

[*] *Monatsh.* 1882, **3**, 205; 1883, **4**, 643.

[†] Burgess, *J.C.S.* 1924, **125**, 2376.

[‡] *J.C.S.* 1895, **67**, 391.

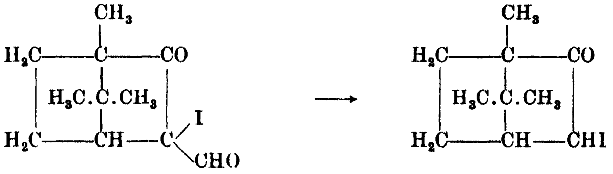
[§] Lapworth, *ibid.* 1899, **75**, 574.

a mixture of *απ-dibromo-α′-nitrocamphor*, m.p. 54°, and *π-bromocamphoric acid* (p. 497).[*] It can be reduced with zinc dust in acetic acid solution to π-bromocamphor.

As in the case of αω-dibromocamphor, an alcoholic solution of απ-dibromocamphor mutarotates ($[\alpha]_D$ +85° to +90°) on the addition of alkali, owing to the formation of *α′π-dibromocamphor*.[†] This isomeride has been prepared by Lowry and Burgess[‡] by the methods adopted for the isolation of similar isomerides. It melts at 182°, $[\alpha]_{5461}$ +111·7° (in acetone, $c = 5$).

Two isomeric tribromocamphors have been described, *αα′ω-tribromocamphor*, m.p. 63–64°, $[\alpha]_D$ +2° (in acetone) and *αα′π-tribromocamphor*, m.p. 69–70°. The former can be prepared by the bromination of αω-dibromocamphor and the latter by the bromination of απ-dibromocamphor.[§]

Only two iodo-derivatives of camphor have been described. *α-Iodocamphor* (XLVIII), m.p. 43–44°, $[\alpha]_D$ +160·42°, was obtained by Haller[‖] by the action of iodine on the sodium derivative of camphor, whilst Brühl[¶] prepared it (*a*) by the action of iodine on camphor in the presence of sodamide, and (*b*) by the action of sodium methoxide on *α-iodo-α-formylcamphor* (XLIX), which can be prepared from hydroxymethylenecamphor (p. 458).


(XLIX) (XLVIII)

αα′-Di-iodocamphor, m.p. 108–109°, $[\alpha]_D$ +28°, was obtained by Brühl[**] by the action of iodine on hydroxymethylenecamphor in the presence of alkali and by the action of sodium hypoiodite on iodoformylcamphor. According to Marsh and Struthers[††] αα′-di-iodocamphor is formed also when either *dimercuricamphor di-iodide*, $C_{10}H_{14}OHg_2I_2$, *tetramercuritricamphor*

---

[*] Lapworth and Kipping, *J.C.S.* 1896, **69**, 308.

[†] Lowry, *ibid.* 1903, **89**, 1037.

[‡] *J.C.S.* 1923, **123**, 1876.

[§] Lapworth, *ibid.* 1899, **75**, 574.

[‖] *Dissertation*, Nancy, 1879; *Compt. rend.* 1875, **80**, 695; 1878, **87**, 695, 843, 929.

[¶] *Ber.* 1904, **37**, 2156.

[**] *Ibid.* 2158.

[††] *J.C.S.* 1909, **95**, 1777; compare Marsh, *ibid.* 1910, **97**, 2410.

di-iodide, $(C_{10}H_{14}O)_3Hg_4I_2$, or *hexamercuripentacamphor di-iodide*, $(C_{10}H_{14}O)_5Hg_6I_2$, are treated with iodine. αα′-Di-iodocamphor is somewhat unstable and, when warmed with sodium methoxide, it yields a mixture of camphor and α-iodocamphor, whilst, when it is treated with magnesium and carbon dioxide, camphor-3-carboxylic acid is obtained.*

NITROCAMPHOR AND ITS DERIVATIVES

Although camphor cannot be directly nitrated, being oxidised by nitric acid (compare p. 394), α′-nitrocamphor can be prepared readily by the reduction of the halogenated nitrocamphors, the preparation of some of which have been described on pp. 399, 401. The study of α′-nitrocamphor and the substituted nitrocamphors has been carried out mainly by Lowry and his collaborators and very interesting results have been obtained.

α′-Nitrocamphor, m.p. 102°, was first prepared by Schiff† by the reduction of α-bromo-α′-nitrocamphor with alcoholic potassium hydroxide, whilst some years later it was obtained by Cazeneuve‡ by the reduction of α-chloro-α′-nitrocamphor with a zinc-copper couple. For the preparation of α′-nitrocamphor, Schiff's method is convenient, the most suitable experimental conditions having been determined by Lowry and Steele.§ It has been obtained also by the reduction of bromonitrocamphor with phenylhydrazine,‖ and by the oxidation of *iso*nitrosocamphor with potassium ferricyanide in alkaline solution.¶

In 1898 Lowry made the important observation that nitrocamphor in benzene solution showed mutarotation, and he later studied this property in great detail, examining both the effects of solvents and of temperature.** He found that in benzene solution the initial value, $[\alpha]_D$ −124°, fell to −104°, and that this change was associated with the presence of the secondary nitro-group (I), since, whilst π-bromo-α′-nitrocamphor (II) also showed mutarotation, α-chloro-α′-nitrocamphor (III) behaved normally. Lowry connected this change in the rotatory power with the conversion of the true nitrocamphor (I) into the *pseudo*-form (IV), but Bell and Sherred* consider that it is more probably due to interconversion of stereoisomers, since the mutarotation is not accompanied by any intensification of the weak coloration given with ferric chloride solution. Although *pseudo*nitrocamphor has not been isolated, it is known in the form of its salts, a number of which have been prepared. These are strongly dextrorotatory, the value for the sodium salt being $[\alpha]_D$ +289°.

---

* Bruhl, *Ber.* 1903, **36**, 4290.

† *Ber.* 1880, **13**, 1403.

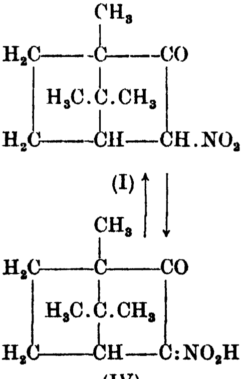
‡ *Bull. Soc. chim.* 1887 [ii], **47**, 920.

§ *J.C.S.* 1915, **107**, 1038; compare Lowry, *ibid.* 1898, **73**, 995.

‖ Forster, *ibid.* 1902, **81**, 868.

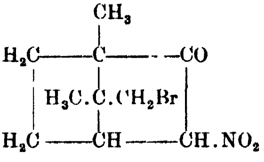
¶ Forster, *ibid.* 1903, **83**, 532.

** *J.C.S.* 1899, **75**, 211; compare Lowry and Robertson, *ibid.* 1904, **85**, 1550.

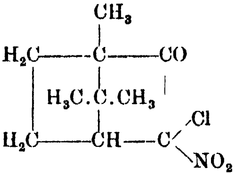


(I)

(IV)



(II)



(III)

When a solution of nitrocamphor is evaporated on the water-bath, the *anhydride* of *pseudo*nitrocamphor (V), m.p. 193°, $[\alpha]_D$ +242°, is obtained.† If this anhydride is heated above its melting-point or digested with alkali, it yields camphorquinone (VI). The tendency for nitrocamphor derivatives to pass into camphorquinone is very marked, since Lapworth‡ has shown that both chloro- and bromo-nitrocamphors give on distillation camphorquinone, and the same change occurs when an alcoholic solution of bromonitrocamphor is exposed to air and light.

By the action of formamide on α′-nitrocamphor, Lowry and Steele§ prepared a second *anhydride*, m.p. 184°, $[\alpha]_{5461}$ − 6°, which has properties very similar to those of the anhydride, m.p. 193°.

---

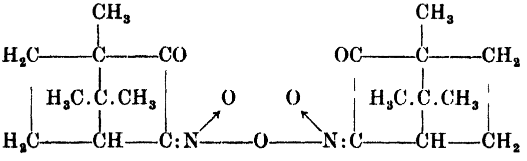
* *J.C.S.* 1940, p. 1202.

† Cazeneuve, *Bull. Soc. chim.* 1889 [iii], **1**, 556; Lowry, *J.C.S.* 1898, **73**, 996.

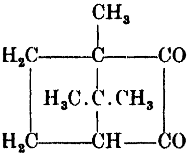
‡ *J.C.S.* 1896, **69**, 322.

§ *Ibid.* 1915, **107**, 1042.

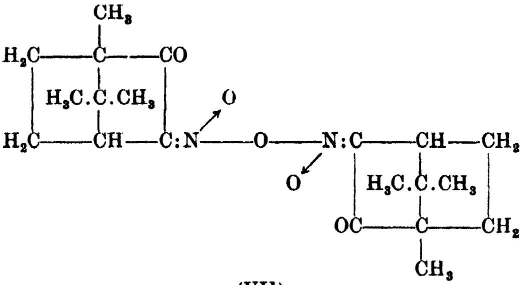
It is possibly the *trans*-modification (VII), the low rotatory power being due to the two nitro-groups acting in opposition to one another.



(V)

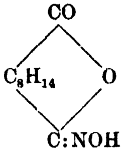


(VI)

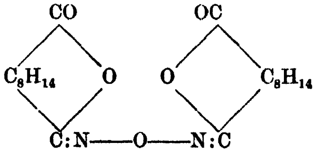


(VII)

α′-Nitrocamphor is readily oxidised by concentrated nitric acid to camphoric acid. When boiled with hydrochloric acid it yields *camphoryloxime* (VIII), m.p. 223°, $[\alpha]_D$ +7·0°, which can be prepared also by the action of hydroxylamine on camphoric anhydride.* At the same time the *anhydride* of this oxime (IX), m.p. 220°, $[\alpha]_D$ +26·4°, is formed. On reduction α′-nitrocamphor yields *α′-aminocamphor* (p. 414).



(VIII)

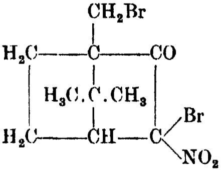


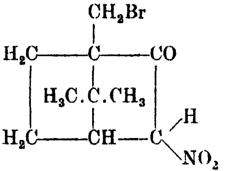
(IX)

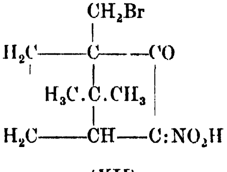
Although *pseudo*nitrocamphor has not been separated in a pure state, two bromo*pseudo*nitrocamphors have been described. When *αω-dibromo-α′-nitrocamphor* (X) is reduced either with alcoholic potassium hydroxide or with sodium ethoxide, *ω-bromonitrocamphor*[*] is obtained, and the crystalline solid, which separates on acidifying the alkaline solution, is a mixture of the true nitro-form (XI) and the *pseudo*-form (XII).

---

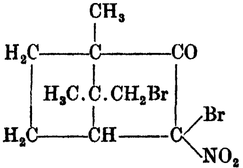
* Cazeneuve, *Bull. Soc. chim.* 1889 [iii], **1**, 417; Lowry, *J.C.S.* 1898, **73**, 1002; 1903, **83**, 957.

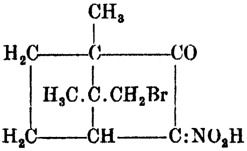

(X)

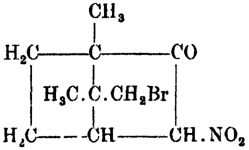

(XI)


(XII)

By careful crystallisation, the pure *pseudo*-nitro compound, m.p. 132°, can be separated, but the normal form cannot be purified and obtained free from the isomeride. In solution ω-bromo-α′-nitrocamphor mutarotates; thus Lowry and Robertson[†] obtained in benzene solution an initial value of $[\alpha]_D$ + 5·8°, and a final value after four days of − 76·7°. ω-Bromo-α′-nitrocamphor does not form an anhydride but, when heated with concentrated hydrochloric acid, *ω-bromocamphoryloxime*, m.p. 112°, $[\alpha]_D$ + 10·2°, is obtained. Very similar properties are shown by *π-bromo-α′-nitrocamphor*, which can be prepared by the reduction of *απ-dibromo-α′-nitrocamphor* (XIII).[‡] The two isomeric forms of π-bromo-α′-nitrocamphor were separated by Lapworth and Kipping and studied in greater detail by Lowry.[§] The *pseudo*-form (XIV), m.p. 142°, crystallised well from chloroform and showed mutarotation, the initial value in benzene solution being $[\alpha]_D$ + 188° and the final value − 38°. The normal form (XV), m.p. 108°, is much more soluble; it has an initial value of $[\alpha]_D$ − 51°, which falls to − 38°. When it is heated with hydrochloric acid it yields *π-bromocamphoryloxime*, m.p. 137–138°, $[\alpha]_D$ + 53°,


(XIII)


(XIV)


(XV)

---

[*] Lowry, *J.C.S.* 1903, **83**, 965.

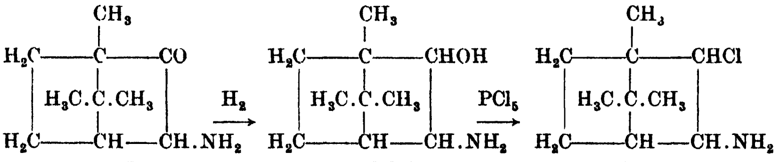
[†] *J.C.S.* 1904, **85**, 1548.

[‡] Lapworth and Kipping, *ibid.* 1896, **69**, 309.

[§] *J.C.S.* 1899, **75**, 223.

which was prepared originally by Lapworth[*] and designated by him *iso*-π-bromonitrocamphor.

By the reduction of α′-nitrocamphor with sodium amalgam in alcoholic solution Schiff[†] prepared *α′-aminocamphor* (XVI). It can be obtained also by the reduction of αω-dibromo-α′-nitrocamphor with zinc dust in acetic acid solution,[‡] by the reduction of *iso*nitrosocamphor with the same reagents,[§] and by the action of ammonia on camphorquinone.[‖] α′-Aminocamphor is a waxy solid, which according to Tiemann[¶] has m.p. 110–115°, b.p. 246·4°. It can be readily characterised by the preparation of its crystalline salts, the *hydrochloride* melting at 223–225°. It yields on reduction with sodium in alcoholic solution *aminoborneol* (XVII), m.p. 187°,[**] from which by the action of phosphorus pentachloride *2-chloro-3-aminocamphane* (XVIII) was prepared.



(XVI) (XVII) (XVIII)

Unlike most α-substituted derivatives of camphor, α′-aminocamphor readily yields a crystalline *oxime*, m.p. 144–145°, $[\alpha]_D + 60{\cdot}5°$.[††] When α′-aminocamphor hydrochloride is treated at 150° with formaldehyde it gives camphorquinone.[‡‡] We are indebted to Forster and his collaborators for a study of a number of interesting derivatives of α′-aminocamphor. It had been observed by Rupe[§§] that when α′-aminocamphor was treated with potassium cyanate it gave *camphorylcarbamide* (XIX), m.p. 169°. By slightly modifying the experimental conditions Forster and Fierz[‖‖] prepared an isomeride, *camphoryl-ψ-carbamide*, m.p. 184°, which undoubtedly has formula (XX), since on treatment with hydroxylamine it gave an *oxime* (XXI), m.p. 202–203°, identical with that which had been prepared by Lapworth and Harvey by the action of potassium cyanate on *α′-aminocamphoroxime* (XXII).

---

[*] *J.C.S.* 1896, **69**, 322.

[†] *Ber.* 1880, **13**, 1404.

[‡] Kachler and Spitzer, *Monatsh.* 1883, **4**, 567.

[§] Claisen and Manasse, *Annalen*, 1893, **274**, 90; Rupe, *Ber.* 1895, **28**, 777; Duden and Pritzkov, *ibid.* 1899, **32**, 1539.

[‖] Rupe and Vignano, *Helv. Chim. Acta*, 1937, **20**, 1078.

[¶] *Ber.* 1897, **30**, 322.

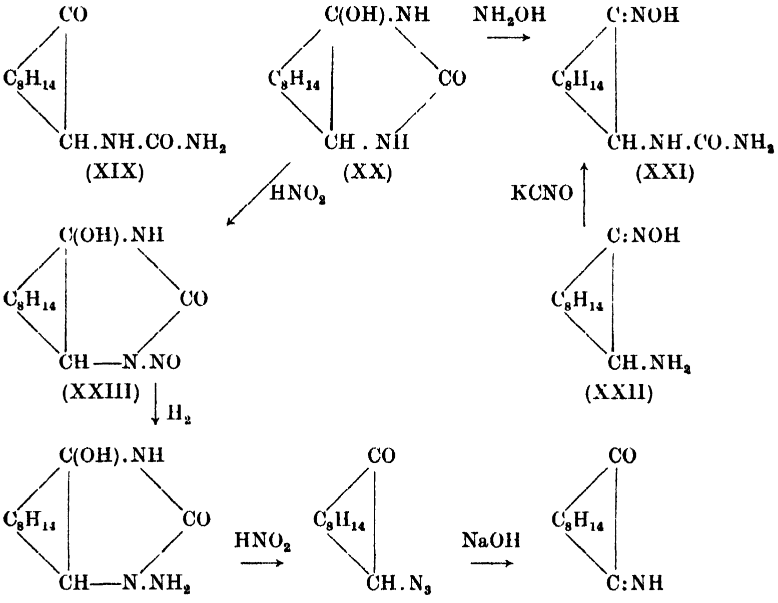
[**] Duden and Macintyre, *ibid.* 1898, **31**, 1902; 1900, **33**, 481.

[††] Lapworth and Harvey, *J.C.S.* 1902, **81**, 550.

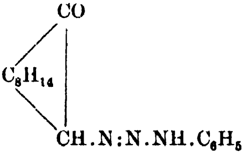
[‡‡] Rupe, Buxtorf and Flatt, *Helv. chim. Acta*, 1930, **13**, 1026.

[§§] *Ber.* 1894, **27**, 584; 1895, **28**, 778.

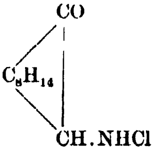
[‖‖] *J.C.S.* 1905, **87**, 110, 718, 826.



(XIX) (XX) (XXI) (XXIII) (XXII) (XXIV) (XXV) (XXVI)



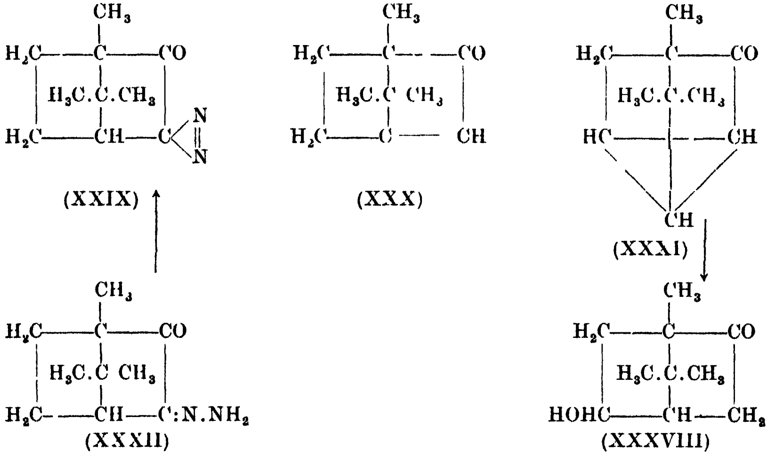
(XXVII)



(XXVIII)

By treatment of camphoryl-*ψ*-carbamide with nitrous acid a *nitroso*-derivative (XXIII) was obtained, which, on reduction with zinc dust, gave *camphoryl-ψ-semicarbazide* (XXIV). This semicarbazide reacted readily with ketones to yield semicarbazones remarkable for their high rotatory power. From the semicarbazide by the action of nitrous acid *camphorylazoimide* (XXV), m.p. 67°, $[\alpha]_D$ −351·5°, was prepared, which gave on treatment with alkali *α-iminocamphor* (XXVI). α′-Aminocamphor reacted with benzenediazonium hydroxide to yield *camphordiazoaminobenzene* (XXVII), m.p. 150°,[*] whilst, by the action of chloramine, N-*chloroaminocamphor* (XXVIII), m.p. 43°, was obtained.[†]

In 1881 Schiff,[‡] by the action of nitrous acid on aminocamphor, prepared *diazocamphor* (XXIX), m.p. 75°, which, when heated, passed into a ketone, $C_{10}H_{14}O$, m.p. 168–170°, characterised by the preparation of an *oxime*, m.p. 132°, and a *semicarbazone*, m.p. 243–244°. This ketone was investigated by Angeli,[§] who concluded that it was the unsaturated ketone (XXX). This formula, in view of the position of the ethylenic linkage, appeared to be very improbable, and the investigations of Bredt and Holz[‖] have shown camphenone to be the tricyclic ketone, β-peri*cyclo*-camphanone (XXXI), which is also termed iso*cyclenone*. A more convenient method for the preparation of the ketone is from *camphorquinonehydrazone* (XXXII), which, by the action of mercuric iodide, gives diazocamphor.



(XXIX)

(XXX)

(XXXI)

(XXXII)

(XXXVIII)

The constitution of the ketone was established in the following manner. When the *oxime* (XXXIV) was digested with acetyl chloride it behaved in an exactly similar manner to camphoroxime (p. 434), ring fission occurring with the formation of the *nitrile* of cyclo*campholenic acid* (XXXV), m.p. 78–80°, which gave on hydrolysis cyclo*campholenic acid* (XXXVI), m.p. 108–110°. By oxidation of the unsaturated acid with potassium permanganate cycloiso*camphoronic acid* (XXXVII), m.p. 228–230°, was prepared. Ring fission may also be brought about by treatment of the ketone with trichloroacetic acid; the product on saponification gives *5-hydroxycamphor* (XXXVIII), m.p. 222°.*

---

[*] Forster and Garland, *J.C.S.* 1909, **95**, 2057.

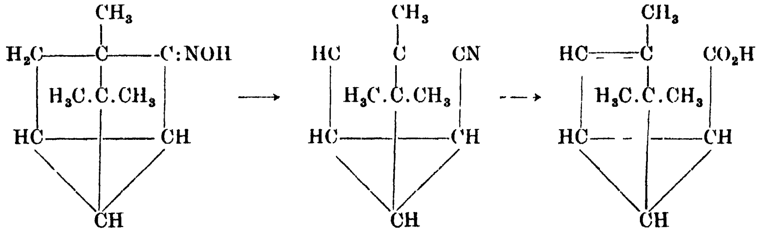
[†] Forster and Schlaepfer, *ibid.* 1914, **105**, 2770.

[‡] *Ber.* 1881, **14**, 1375.

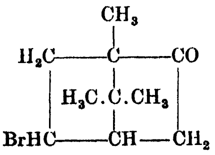
[§] *Gazzetta*, 1894, **24**, II, 44; *Ber.* 1895, **28**, 819.

[‖] *J. pr. Chem.* 1917 [II], **95**, 133; see also Ishidate and Isshiki, *Bull. C.S. Japan*, 1942, **17**, 502.

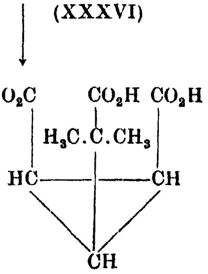
On reduction, β-peri*cyclo*camphanone yields the corresponding alcohol, *β-peri*cyclo*camphanol*, m.p. 174–176°,† $[\alpha]_D$ +36·69°, *phenylurethane*, m.p. 106–108°; from the *hydrazone*, m.p. 77°,‡ *peri*cyclo*camphane*, m.p. 117–118°, was prepared by Kishner's method. When β-peri*cyclo*camphanone is treated with hydrogen bromide it yields a bromocamphor, m.p. 114°, $[\alpha]_D$ +13·23°, which is probably *5-bromocamphor* (XXXIX). On bromination, a dibromocamphor, m.p. 58–59°, is formed, but this has not been orientated.



(XXXIV) (XXXV) (XXXVI)



(XXXIX)



(XXXVII)

---

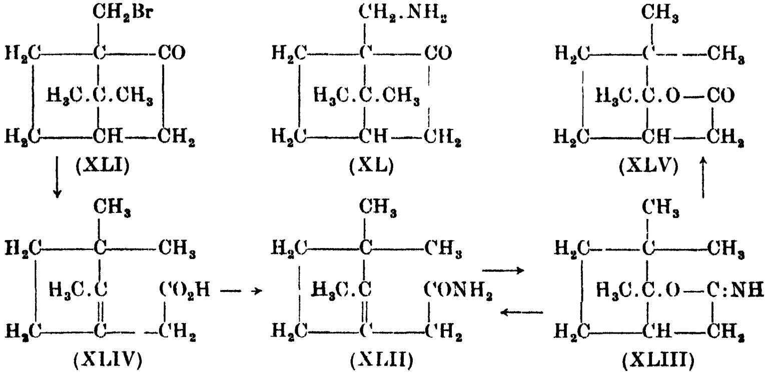
* Takeuchi, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1934, **23**, 288.

† Since this alcohol is capable of existing in stereoisomeric modifications, the recorded melting-points are somewhat variable. Lipp, Oeckinghaus and Conze (*Ber.* 1941, **74**, 6) recorded m.p. 180–181° (3:5-*dinitrobenzoate*, m.p. 116°) for a specimen obtained by hydrogenation of the ketone.

‡ Compare Briussova, *J. Gen. Chem. Russ.* 1936, **6**, 667.

α′-Aminocamphor has been used in a number of synthetical operations more especially by Duden and his collaborators, for an account of which the original literature should be consulted; of particular interest is the formation of pyrazines.[*]

In 1895 Tiemann[†] described a substance termed *iso*aminocamphor, m.p. 39°, which was isomeric with α′-aminocamphor. This was prepared by the action of hydrogen iodide on camphoroxime and also by the action of this reagent on α- or β-campholenamide. Forster and Howard[‡] concluded that it was *ω-aminocamphor* (XL) since it could be prepared by the action of ammonia on ω-bromocamphor (XLI); when distilled at the ordinary pressure it gave *β-campholenamide* (XLII). More recently, however, Asahina and Tsukamoto[§] have shown that the substance is not a true amine, and is probably *dihydro-β-campholeno-iminolactone* (XLIII). Its formation by the action of ammonia on ω-bromocamphor is explained by the intermediate transformation of the latter into β-campholenic acid (XLIV), a change which is known to occur in the presence of alkali. The conversion of "*iso*aminocamphor" into dihydrocampholenolactone (XLV) on boiling with water is also readily understandable.



A number of *amino-acids* and *betaines* of the camphor series have been prepared by Rupe and Martin.[||]

---

[*] Compare Rupe and Vignano, *Helv. Chim. Acta*, 1937, **20**, 1078.

[†] *Ber.* 1895, **28**, 1082; 1897, **30**, 321.

[‡] *J.C.S.* 1913, **103**, 63.

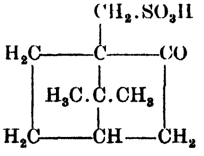
[§] *Ber.* 1938, **71**, 305.

[||] *Helv. Chim. Acta*, 1934, **17**, 1263.

THE CAMPHOR-SULPHONIC ACIDS

Although by the action of sulphuric acid on camphor and its derivatives degradation either to alicyclic ketones or aromatic phenols may result, it has been found possible to prepare camphor- and substituted camphor-sulphonic acids. The introduction of these acids by Pope in 1898 for the resolution of externally compensated basic compounds has been of very great value in the development of stereochemistry.

By the action of sulphuric acid on camphor dissolved in acetic anhydride Reychler[*] prepared a sulphonic acid which crystallised from either ethyl acetate or acetic acid in prisms, m.p. 193–195°, and consisted of d-*camphor* ω- (or 10-) *sulphonic acid.* The constitution of this acid was established later as the result of the investigations of Armstrong and Lowry,[†] Bredt, Rochussen and Heusch,[‡] Wedekind, Schenk and Stüsser,[§] Lipp and Lausberg[||] and Burgess and Lowry,[¶] and, for the reasons detailed on p. 389, there can be no doubt that it must be represented by formula (I). The acid can be characterised by the preparation of the *oxime*, m.p. 177–178°.



(I)

By the sulphonation of *l*-camphor and *dl*-camphor the corresponding laevorotatory and externally compensated sulphonic acids have been prepared. The latter was first resolved into its optical enantiomorphs by Rewald,[**] the optimum conditions for effecting this resolution having been determined by Burgess and Gibson.[††] The following rotatory powers have been quoted for the acids: $[\alpha]_{5461}$ +28·27°, −28·3°. The reactions of the acid have been studied in some detail. Like other derivatives of camphor containing the substituent in the ω-position it passes readily into α-campholenic acid, the change in the case of the sulphonic acid being most readily effected by fusion with potassium hydroxide.[*] When reduced with sodium in alcoholic solution a mixture of the two stereoisomeric forms of the *hydroxy-acid* (II) is formed, which on dehydration gives a *sultone*, m.p. 133·5°, a substance which can also be prepared by the treatment of camphene (III) with sulphur trioxide in acetic acid solution. Lipp and Holl[†] assigned formula (IV) to the sultone, but according to Asahina, Sano and Mayekawa[‡] the substance is actually an *iso*camphane derivative, and is to be represented by formula (V); it may also be obtained by dehydration of *2-hydroxycamphane-π-sulphonic* acid (VI). A Wagner change is involved in the formation of the sultone from either of the hydroxysulphonic acids (II) and (VI); in addition, a rearrangement of the Nametkin type (see p. 162) must occur in the former instance.

---

[*] *Bull. Soc. chim.* 1898 [iii], **19**, 120.

[†] *J.C.S.* 1902, **81**, 1444.

[‡] *Ber.* 1902, **35**, 1290.

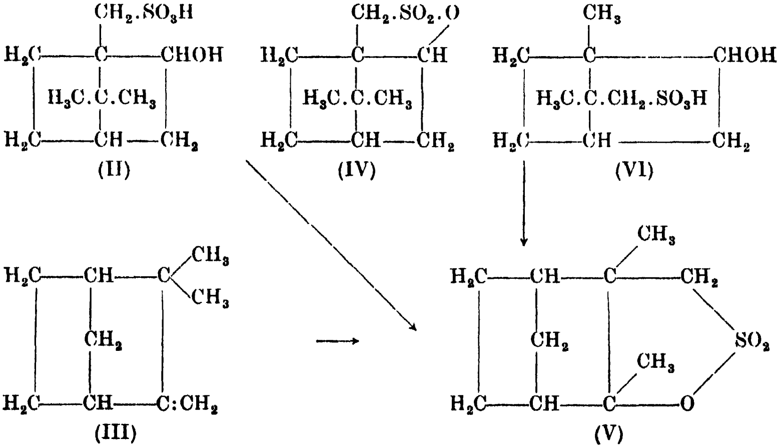
[§] *Ibid.* 1922, **56**, 640.

[||] *Annalen*, 1924, **436**, 274.

[¶] *J.C.S.* 1925, **127**, 279.

[**] *Ber.* 1909, **42**, 3136.

[††] *J.S.C.I.* 1925, **44**, 296.



It was observed by Reychler that when *camphor-ω-sulphonyl chloride*, m.p. 67–68°, was treated with ammonia two amides were formed. These were subsequently investigated by Armstrong and Lowry[§] and by Lowry and Magson.[||] One of them was found to be the normal *amide* (VII), m.p. 132°, whilst the second was an *anhydramide* (VIII), m.p. 223°. The conversion of the amide into the anhydramide takes place with remarkable facility, the addition of a trace of alkali being sufficient to occasion the change. Some further reactions of the anhydramide have been described by Shriner, Shotton and Sutherland.* When hydrogenated in the presence of nickel it gives the *sultam* (IX), which, although theoretically capable of existing in two stereoisomeric modifications, was isolated as a single form, m.p. 181–182°. On methylation with methyl iodide, the N-*methylsultam* (X), m.p. 80°, was obtained, which underwent ring scission on treatment with concentrated hydrochloric acid to give 2-(N-*methylamino*)-*camphane-ω-sulphonic acid* (XI), m.p. 325–326°. This substance,

---

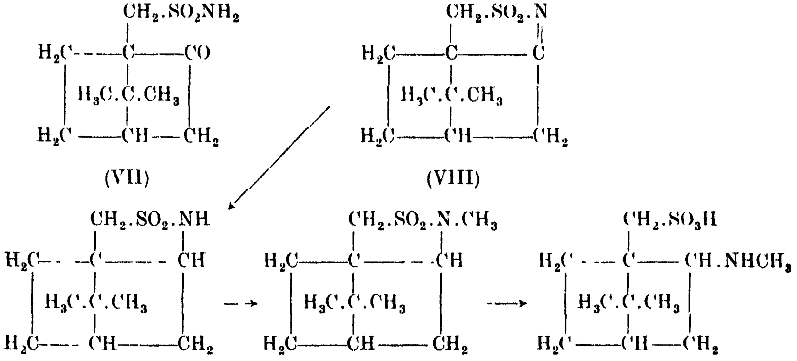
[*] Bredt, Rochussen and Heusch, *Ber.* 1902, **35**, 1290.

[†] *Ber.* 1929, **62**, 499.

[‡] *Ibid.* 1938, **71**, 313.

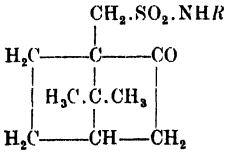
[§] *J.C.S.* 1902, **81**, 1448.

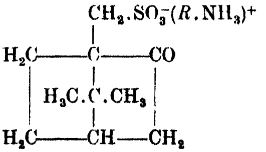
[||] *Ibid.* 1906, **89**, 1046.

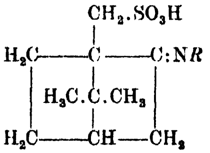

(VII) (VIII)

(IX) (X) (XI)

which on dehydration is reconverted into (X), has also been encountered by Shriner in his investigations on the structures of the amine salts of camphor-ω-sulphonic acid.† The anomalous mutarotation displayed by the salts (XII) formed with primary amines suggested that on dehydration they were capable of reacting in the ketimine form (XIII) rather than as the sulphonamide (XIV).


(XIV)


(XII)


(XIII)

---

* *J. Amer. C.S.* 1938, **60**, 2794.

† Shriner *et al.*, *J. Amer. C.S.* 1935, **57**, 1306, 1445, 1896; 1936, **58**, 62; 1938, **60**, 1314.

By dehydration of the methylamine salt, the ketimine (XIII, $R=CH_3$), m.p. 312–313°, was obtained, the structure of which was proved by hydrogenation to be a mixture of two stereoisomers, one of which was identical with the *N*-methylamino compound (XI).

Similarly, dehydration of the aniline salt gave a *phenylketimine* (XIII, $R=C_6H_5$), m.p. 294–295°, from which the *N*-phenyl analogues of (X) and (XI) were prepared. The true *anilide* (XIV, $R=C_6H_5$) of camphor-ω-sulphonic acid can be obtained by treatment of the sulphonyl chloride with aniline; it has m.p. 121°, $[\alpha]_D^{25^\circ}$ $+76^\circ$ (in chloroform) and shows no mutarotation.

As was mentioned on p. 387, when camphor-ω-sulphonylbromide is heated to about 130° it yields ω-bromocamphor; the corresponding chloride cannot, however, be prepared in a similar manner from the sulphochloride. *α-Chloro-* and *α-bromo-camphor-ω-sulphonic acids* have been obtained by the sulphonation of α-chloro- and α-bromo-camphors.[*] According to Pope and Read,[†] who have determined the rotatory power of a number of its salts, the bromosulphonic acid melts at 47·5°.

When *d*-camphor is treated with either fuming sulphuric acid or chlorosulphonic acid dl-*camphor-π-sulphonic acid* (XV) is obtained, camphor being racemised during the reaction.[‡] The acid can be purified by conversion into the crystalline *sulphonyl chloride*, m.p. 105·5–106·5°, and characterised by the preparation of the *amide*, m.p. 133·5–136·5°[§]. Whilst the direct sulphonation of camphor gives the externally compensated acid, the optically active modifications can be prepared by the reduction of the *d*- and *l*-α-bromocamphor-π-sulphonic acids.[||] With the aid of strychnine, Pope and Read[¶] resolved the externally compensated acid and found the ammonium salts of the active acids to have the rotatory powers $[\alpha]_D$ $+80{\cdot}5^\circ$ and $-80{\cdot}1^\circ$ in alcoholic solution.

---

[*] Armstrong and Lowry, *J.C.S.* 1902, **81**, 1451; Lowry and Magson, *ibid.* 1906, **89**, 1047.

[†] *Ibid.* 1914, **105**, 800.

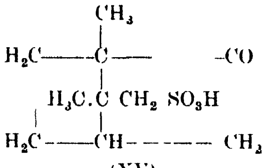
[‡] Kipping and Pope, *ibid.* 1893, **63**, 549; 1895, **67**, 357. According to Poggi and Pasquarelli (*Ann. Chim. applicata*, 1947, **37**, 321; 1948, **38**, 71) the best results are obtained by the use of methyl chlorosulphonate.

[§] Several *N*-substituted camphor-π-sulphonamides have been described by Mousseron, Granger and Claret (*Bull. Soc. Chim.* 1947 [v], **14**, 868).

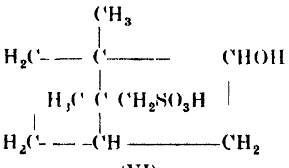
[||] Kipping and Pope, *ibid.* 1896, **69**, 358; Kipping, *ibid.* 1901, **79**, 372.

[¶] *Ibid.* 1910, **97**, 992.

By the reduction of camphor-π-sulphonic acid with sodium and alcohol, Asahina, Sano and Mayekawa[*] obtained the sodium salt of *2-hydroxycamphane-π-sulphonic acid* (VI); on treatment with hydrochloric acid this was converted into the *sultone*, m.p. 133°, to which reference has already been made on p. 420.

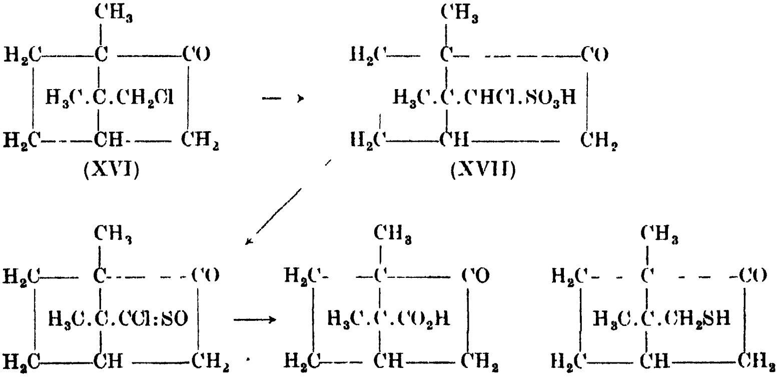


(XV)



(VI)

When *dl*-camphor-π-sulphonyl chloride is heated to 190° it yields *π-chlorocamphor* (XVI) which on resulphonation gives *π-chlorocamphor-π-sulphonic acid* (XVII). This was converted by Wedekind and Stüsser[†] into the *chlorosulphoxide* (XVIII), m.p. 190°, which on oxidation with permanganate gave iso*ketopinic acid* (XIX), m.p. 250°. A similar reaction has been carried out by Hasselström on the *bromosulphoxide*, m.p. 137°.



(XVI) (XVII) (XVIII) (XIX) (XX)

Reduction of camphor-π-sulphonyl chloride with tin and hydrochloric acid gives *camphor-π-thiol* (XX), m.p. 94°, $[\alpha]_D^{22°}$ + 108·7°, which can be oxidised to the *disulphide*, m.p. 215°.[§]

---

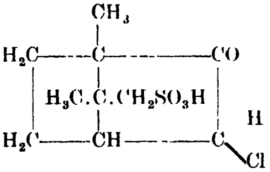
[*] *Ber.* 1938, **71**, 312.

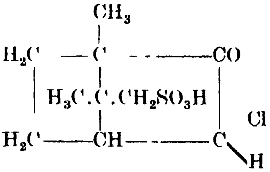
[†] *Ibid.* 1923, **56**, 1557.

[‡] *Annal. Acad. Sci. Fennicae*, 1929, A, **30**, no. 12.

[§] Tukamoto, *J. Pharm. Soc. Japan*, 1939, **59**, 37.

By the sulphonation of α-chloro-*d*-camphor with fuming sulphuric acid, Kipping and Pope[*] prepared α-chloro-*d*-camphor-π-sulphonic acid, m.p. 185°. Although the acid so obtained was apparently homogeneous, the investigations of Kipping and his collaborators[†] have shown conclusively that it is actually a mixture of *α-chloro-* and *α′-chloro-*d*-camphor-π-sulphonic acids* (XXI) and (XXIa), although neither of these acids has been obtained pure.[‡]


(XXI)


(XXIa)

The *sulphonyl chloride* melts at 123–124° and the *sulphonyl bromide* at 145°; on heating to about 150° they yield respectively *απ-dichloro-* and *α-chloro-π-bromocamphors.*

The related *α-bromocamphor-π-sulphonic acid* was prepared by Kipping and Pope[§] by the sulphonation of α-bromocamphor and, like the chloro-acid, it is probably a mixture of α-bromo-*d*-camphor-π-sulphonic acid and α′-bromo-*d*-camphor-π-sulphonic acid. These acids have not been separated, but their hydrindamine salts have probably been obtained pure.[‖] α-Bromo-*d*-camphor-π-sulphonic acid has m.p. 195–196°, $[\alpha]_D$ +88·27°. The *amide*, m.p. 145°, shows mutarotation in alcoholic solution in the presence of a trace of alkali, thus behaving in a similar manner to other α-substituted camphors.[¶] The properties of this acid, which has been used extensively in the resolution of externally compensated bases, have been very thoroughly investigated and it is only possible to refer to a few of the more important of its reactions. By oxidation of the ammonium salt with potassium permanganate, Lapworth and Kipping[**] obtained d-*camphoric*

---

[*] *J.C.S.* 1893, **63**, 593.

[†] *Ibid.* 1905, **87**, 628, where full references to the literature are given.

[‡] Kipping, *Proc. C.S.* 1905, **21**, 293.

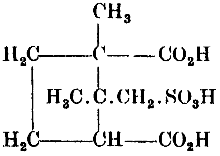
[§] *J.C.S.* 1893, **63**, 577; compare Ingersoll and Babcock, *J. Amer. C.S.* 1933, **55**, 341; Regler and Hein, *J. pr. Chem.* 1937 [ii], **148**, 1.

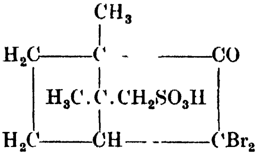
[‖] Kipping, *Proc. C.S.* 1905, **21**, 124.

[¶] Compare Lowry and Magson, *J.C.S.* 1906, **89**. 1045.

[**] *J.C.S.* 1897, **71**, 8.

acid-π-sulphonic acid (XXII), the same acid being obtained by oxidation with nitric acid. If, however, concentrated nitric acid be used, then, in addition to this acid, *αα′-dibromocamphor-π-sulphonic acid* (XXIII), m.p. 245–252°, and *αα′-dibromocamphor-π-sulpholactone*, m.p. 188–189°, are obtained.* The dibromo-acid can, however, be prepared more conveniently by bromination of the ammonium salt of the sulphonic acid. By heating the sulphonyl chloride and sulphonyl bromide, *π-chloro-α-bromocamphor* and *απ-dibromocamphor* are formed.


(XXII)

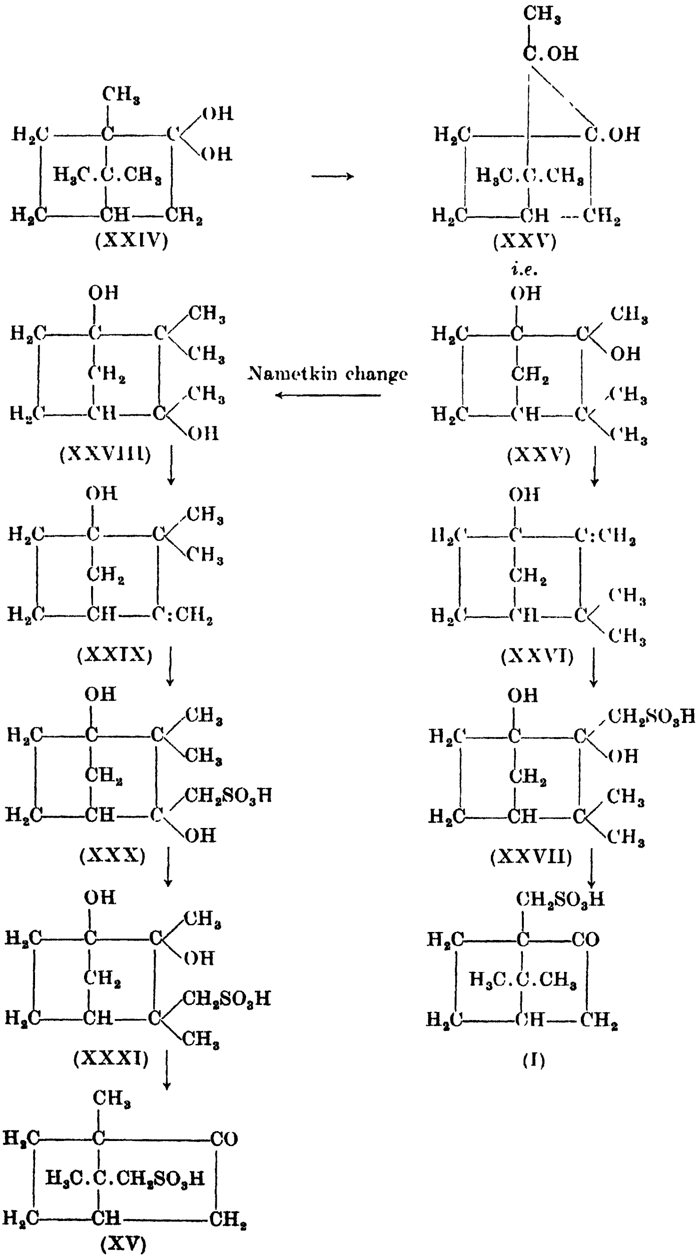

(XXIII)

The mechanism of the sulphonation of camphor, particularly in view of the controversy concerning the structure of the "β"-sulphonic acid (p. 389), is of considerable interest, but it is only comparatively recently, with the recognition of the Nametkin type of isomerisation, that it has been possible to suggest a simple series of changes which will explain the formation of the ω- and of the π-acids. Asahina† suggests that camphor, in the form of its hydrate (XXIV), undergoes a Wagner rearrangement to 1-hydroxycamphene hydrate (XXV), which then dehydrates to give 1-hydroxycamphene (XXVI): this then adds sulphuric acid to form (XXVII), which by a further Wagner rearrangement is transformed into camphor-ω-sulphonic acid (I). If on the other hand the conditions are such that the 1-hydroxycamphene hydrate (XXV) can undergo a Nametkin transformation into 4-hydroxycamphene hydrate (XXVIII), this would then dehydrate to give 4-hydroxycamphene (XXIX) which would add sulphuric acid to form (XXX). A second Nametkin rearrangement then gives (XXXI) which after a final Wagner change results in the formation of the π-sulphonic acid (XV). Support for the first part of the scheme is provided by the

---

* Lapworth, *J.C.S.* 1899, **75**, 559.

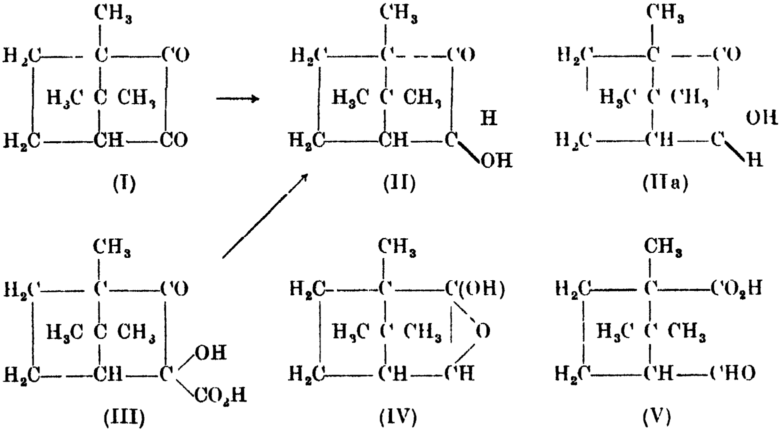
† *Proc. Imp. Acad. Tokyo*, 1937, **13**, 38; compare Lipp and Knapp, *Ber.* 1940, **73**, 915.


(XXIV)
(XXV)
i.e.
(XXVIII)
Nametkin change
(XXV)
(XXIX)
(XXVI)
(XXX)
(XXVII)
(XXXI)
(I)
(XV)

observation that 1-hydroxycamphene on treatment with sulphuric acid gives the ω-sulphonic acid more rapidly than camphor under the same conditions. It is, of course, improbable that the hydrates (XXIV), (XXV) and (XXVIII) could exist as such under the conditions of sulphonation, but they could equally well be replaced by sulphates or acetates in the above scheme.

THE HYDROXYCAMPHORS

The existence of a number of structurally isomeric hydroxycamphors is possible, and all except one (6-hydroxycamphor) have been described. In 1897 Manasse[*] obtained by the reduction of camphorquinone (I) with zinc dust in acetic acid solution two isomeric hydroxycamphors, $C_{10}H_{16}O_2$, m.p. 203–205° and 212–213°, which he designated, somewhat unfortunately, α- and β-hydroxycamphors, and he regarded them as stereoisomerides having the structures (II) and (IIa). Subsequently α-hydroxycamphor was prepared by Lapworth and Chapman[†] by heating


(I) (II) (IIa)
(III) (IV) (V)

hydroxycamphorcarboxylic acid (III) above its melting-point. This method of preparation left no doubt that α-hydroxycamphor was a true derivative of camphor. Since, in many of their reactions, the two hydroxycamphors did not behave as if they were stereoisomerides, they were studied simultaneously by Karrer and Takashima[*] and by Forster and Shukla,[†] who independently concluded that the β-hydroxycamphor was the *oxide* (IV). A prolonged reinvestigation by Bredt and his collaborators[‡] has shown this to be incorrect. α-Hydroxycamphor, *d*-, m.p. 197–198°, $[\alpha]_D$ +17·3°, *semicarbazone*, m.p. 183–184°, *dl*-, m.p. 200°, *semicarbazone*, m.p. 182–183°, is a true hydroxycamphor (II), since it gives on reduction with sodium amalgam *d*-camphor.[§] On oxidation with lead tetra-acetate in the presence of water it gives *camphoric acid sec.-semialdehyde* (V), m.p. 126–127·5°, $[\alpha]_D^{20°}$ +38° (in benzene), 2.4-*dinitrophenylhydrazone*, m.p. 224°, *oxime*, m.p. 142–143·5°, *semicarbazone*, m.p. 199°.[‖] α-Hydroxycamphor can theoretically exist in two stereoisomeric modifications, and Rupe and Muller[¶] by the hydrogenation of camphorquinone have obtained a stereoisomer, m.p. 210–211°, $[\alpha]_D^{20°}$ +115·6° (*semicarbazone*, m.p. 199–201°).

---

[*] *Ber.* 1897, **30**, 659.

[†] *J.C.S.* 1901, **79**, 384.

β-Hydroxycamphor, *d*-, m.p. 211°, $[\alpha]_D$ +9·05°, *dl*-, m.p. 211–213°, *semicarbazone*, m.p. 215–216°, can be most conveniently separated from the α-isomeride by etherification, when it yields a sparingly soluble dimolecular *methyl ether*, m.p. 37–38°. It forms the sole product when camphorquinone is reduced with aluminium amalgam in ethereal solution. Unlike α-hydroxycamphor, on reduction with sodium amalgam it does not yield camphor, but epicamphor (VI), and it is therefore the structural isomeride, 2-*hydroxyepicamphor* (VII); on oxidation with lead tetra-acetate in the presence of water it gives *camphoric acid* tert.-*semialdehyde* (VIII), m.p. 76–77·5°, $[\alpha]_D^{20°}$ +112·2° (in benzene), 2:4-*dinitrophenylhydrazone*, m.p. 220°, *oxime*, m.p. 160–161°, *semicarbazone*, m.p. 204·5–206°.[**] It apparently owes its formation to the reduction of camphorquinone proceeding in accordance with the scheme:

---

[*] *Helv. Chem. Acta*, 1925, **8**, 242.

[†] *J.C.S.* 1925, **127**, 1855.

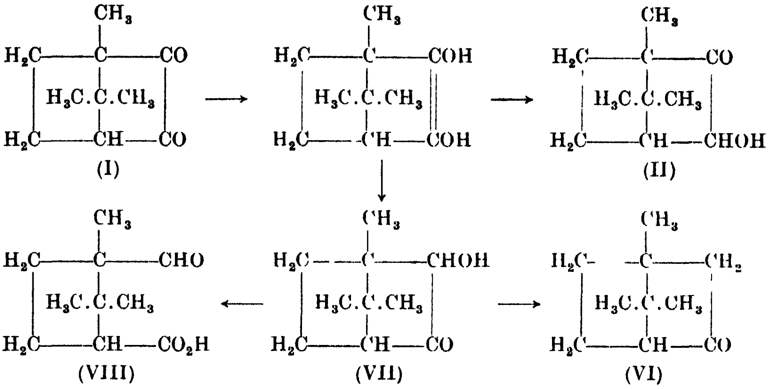
[‡] Bredt and Ahrens, *J. pr. Chem.* 1926 [II], **112**, 273; Bredt, *ibid.* 1929 [II], **121**, 153; Bredt and Bredt-Savelsberg, *Ber.* 1929, **62**, 2214; Bredt and Fischer, *J. pr. Chem.* 1931 [II], **131**, 49.

[§] Ishidate, *J. Pharm. Soc. Japan*, 1928, **48**, no. 5, 77.

[‖] Baer, *J. Amer. C.S.* 1942, **64**, 1416.

[¶] *Helv. Chim. Acta*, 1941, **24**, 265 E.

[**] Baer, *J. Amer. C.S.* 1942, **64**, 1416.



It is of interest to note that 2-hydroxyepicamphor is largely converted into 3-hydroxycamphor (II) when it is digested with alkali, the salt of the dienol in this case also being an intermediate stage in the reaction.[*]

The urine of dogs which have received food containing camphor was considered by Schmiedeberg and Meyer[†] and by Magnus-Levy[‡] to contain a hydroxycamphor, which was excreted in combination with glucuronic acid.[§] The hydroxycamphor (campherol), prepared from this by hydrolysis, has been shown by Asahina and Ishidate[||] to be a mixture of 3-hydroxycamphor (Manasse's α-hydroxycamphor), 5-*hydroxycamphor* (IX) and π-(8- or 9-) *hydroxycamphor* (X).

5-Hydroxycamphor, m.p. 225°, $[\alpha]_D^{25^\circ}$ +43·8° (in alcohol), p-*nitrobenzoate*, m.p. 158–159°, *semicarbazone*, m.p. 233°, on oxidation gave p-*diketocamphane* (XI), m.p. 210–212°, $[\alpha]_D^{18^\circ}$ +106°, which had been prepared by Bredt and Goeb[¶] by the oxidation of 6-hydroxyepicamphor,[**] and also by the oxidation of camphor with chromic acid. Reduction of the diketone with sodium and alcohol[*] regenerates 5-hydroxycamphor; further reduction, with sodium amalgam, gives camphor. The hydroxyketone is also formed by the hydrolytic fission of the *cyclo*propane ring in *β-pericyclocamphanone* (XII).[†] When the semicarbazone is reduced by the Kishner-Wolff method with sodium ethoxide, it gives epiborneol (XIII).

---

[*] Bredt and Fischer, *J. pr. Chem.* 1931 [ii], **131**, 56.

[†] *Z. phys. Chem.* 1879, **3**, 422.

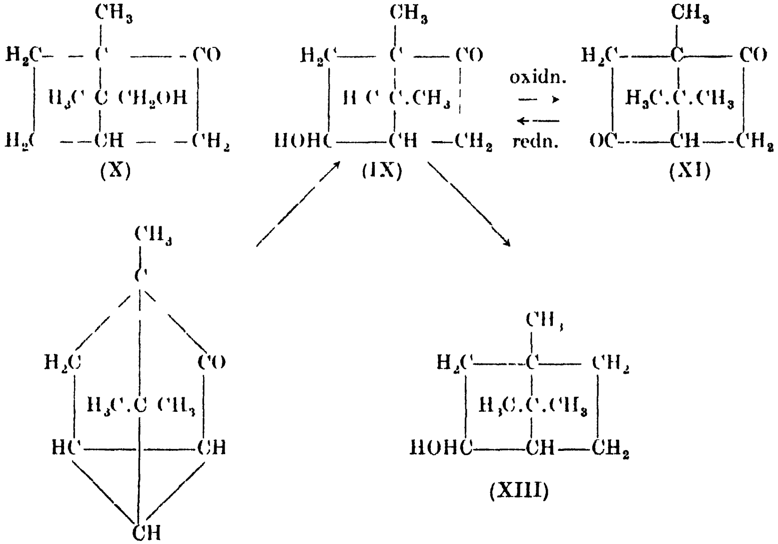
[‡] *Biochem. Z.* 1907, **2**, 319.

[§] For further details regarding the products obtained from feeding experiments with camphor and its derivatives, reference should be made to the following papers: Asahina and Ishidate, *Ber.* 1935, **68**, 947; Ishidate, Kawahata and Nakazawa, *ibid.* 1941, **74**, 1707; Reinartz *et al.*, *ibid.* 1934, **67**, 548, 589, 1536; 1935, **68**, 310; 1939, **72**, 1; Sahashi *et al.*, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1934, **25**, 47.

[||] *Ber.* 1928, **61**, 533; 1931, **64**, 188; 1933, **66**, 1673.

[¶] *J. pr. Chem.* 1920 [ii], **101**, 273.

[**] Prepared by the oxidation of borneol (see p. 361).



(X) (IX) (XI) (XII) (XIII)

d-trans-*π-Hydroxycamphor* (X), m.p. 233°, $[\alpha]_D^{15^\circ}$ $+62{\cdot}2^\circ$ (in alcohol), *semicarbazone*, m.p. 224–225°, identical with that isolated from campherol, has been obtained synthetically by Asahina and Ishidate[‡] by the reduction of the methyl ester of *iso*ketopinic acid (*trans-π*-apocamphor-7-carboxylic acid) (XIV)[§] with sodium and alcohol, and also by the treatment of *π-bromocamphor* (XV) with potassium acetate, followed by saponification.* The *dl*-form also melts at 233°. d-cis-π-*Hydroxycamphor* (Xa), m.p. 233°, $[\alpha]_D^{15°}$ +40·7° (in alcohol), *semicarbazone*, m.p. 216–217°, is prepared from the *cis*-form of (XIV). On oxidation with chromic acid, the respective π-*formyl*-π-*apocamphors* are obtained: *trans*-, m.p. 204–205°, *disemicarbazone*, m.p. 340°; cis-, (XVI), m.p. 205°, *disemicarbazone*, m.p. 256°. Reduction of the semicarbazones of *trans*- and of *cis*-π-hydroxycamphors with sodium ethoxide gives respectively d- and l-π-*borneol* (XVII) (*dihydroteresantalol*) (see p. 270), m.p. 200·5°, $[\alpha]_D^{16°}$ +17·7°, −16·8° (in alcohol), which on oxidation give π-*camphor* (XVIII)

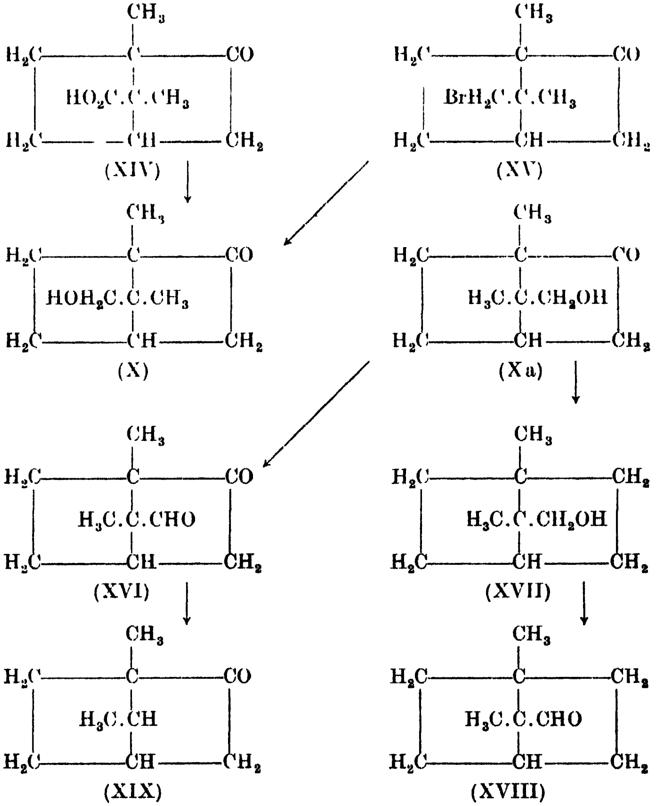
---

[*] This preferential reactivity of the 5-keto group is shown also by the formation of a 5-*monosemicarbazone*, m.p. 238–240°, the structure of which is proved by Kishner-Wolff reduction to borneol (Asahina and Ishidate, *Ber.* 1934, **67**, 71). If, however, 2:5-diketocamphane is hydrogenated over platinum, it gives 2:5-*dihydroxycamphane* (5-*hydroxyborneol*), m.p. 263° (Alder and Stein, *Annalen*, 1936, **525**, 221).

[†] Takeuchi, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1934, **23**, 288; **25**, 66.

[‡] *Ber.* 1934, **67**, 71.

[§] For practical reasons, the reduction was actually carried out on the semicarbazone.

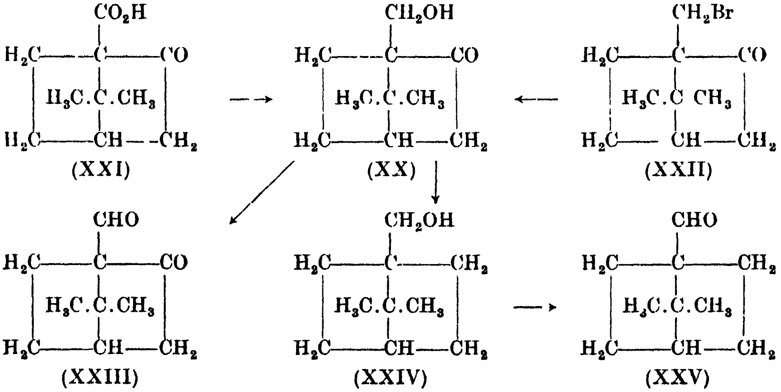


---

* Sahashi and Iki, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, 1934, **25**, 73; compare Asahina and Ishidate, *Ber.* 1935, **68**, 947.

(*dihydroteresantalal*), m.p. 172–173° (*semicarbazone*, m.p. 214–215°). When left in contact with water, in the absence of oxygen, π-formyl-π-apocamphor undergoes a remarkable cleavage of the aldehydic group, which is liberated as formic acid, resulting in the formation of santenone (XIX).[*]

d-ω- (10-) *Hydroxycamphor*[†] (XX), m.p. 220°, $[\alpha]_D^{16°}$ +48·6° (in alcohol), *semicarbazone*, m.p. 213°, has been obtained by reduction of the methyl ester of ketopinic acid (XXI) with sodium and alcohol[‡] and also by treatment of *ω-bromocamphor* (XXII) with potassium acetate, followed by saponification of the ester.[§] On oxidation with chromic acid it gives the aldehydo-ketone (XXIII) (*ω-ketocamphor*), m.p. 210–213°, $[\alpha]_D^{25°}$ +75° (in alcohol), whilst reduction of its semicarbazone with sodium ethoxide gives *ω-borneol* (XXIV), m.p. 200–201°, oxidised to *ω-camphor* (XXV), m.p. 187–189°.


(XXI) (XX) (XXII) (XXIII) (XXIV) (XXV)

1-4-*Hydroxycamphor* (XXVI), m.p. 250°, $[\alpha]_D^{17°}$ −16°, has been obtained by Houben and Pfankuch[‖] from the *amide* of *camphor-4-carboxylic acid* (XXVII), m.p. 207–208°, which is converted into 4-*aminocamphor* (XXVIII), m.p. 230–232°, the latter compound then being treated with nitrous acid. Owing to the tertiary nature of the hydroxyl group, the substance is very stable towards oxidation with chromic acid.

---

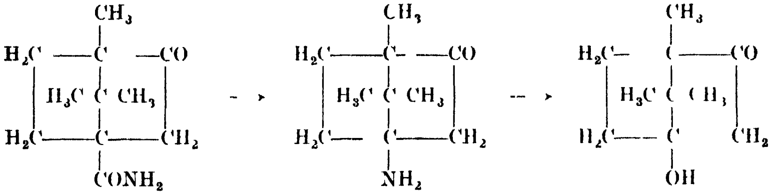
[*] Ishidate and Sano, *Ber.* 1941, **74**, 1189.

[†] The substance designated "β"-hydroxycamphor by Forster and Howard (*J.C.S.* 1913, **103**, 63) was formulated by them on the basis of a similar structure postulated for "*iso*aminocamphor". This has now been shown to be erroneous (see p. 418), and it is very doubtful whether their substance was actually a hydroxycamphor.

[‡] Asahina and Ishidate, *Ber.* 1934, **67**, 1202.

[§] Iki, *Sci. Pap. Inst. Phys. Chem. Res. Tokyo,* 1934, **25**, 78.

[‖] *Annalen*, 1931, **489**, 193.



(XXVII) (XXVIII) (XXVI)

SOME REACTIONS INVOLVING THE CARBONYL GROUP

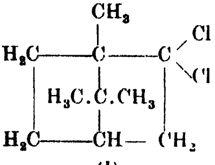
Although, when camphor is warmed with phosphorus pentachloride, it undergoes decomposition with the formation of *p*-cymene and carvacrol, this reagent can react normally and cause the replacement of the oxygen atom of the carbonyl group by chlorine. Since the pioneering experiments of Gerhardt,* the reaction has been the subject of numerous investigations,† but it is only comparatively recently that a clear insight into the mechanism of the reaction has been obtained and the products which are formed isolated in a state of purity. It has been shown by Meerwein and Wortmann‡ that, under very carefully defined conditions, camphor reacts with phosphorus pentachloride to yield *α-camphor dichloride* (*α-dichlorocamphane*) (2.2-*dichlorocamphane*) (I), m.p. 155-156°, the products described by previous investigators being mixtures. The difficulty in separating this dichloride is due to its tendency to undergo the pinacon-pinacolin rearrangement. If it is allowed to stand in toluene solution with stannous chloride, it is isomerised to *β-camphor dichloride* (*β-dichlorocamphane*), m.p. 178–179°, which is obtained also if the temperature is allowed to rise during the interaction of camphor and phosphorus pentachloride. Although this chloride was formulated by Meerwein and Wortmann as 2:6-dichlorocamphane (II), more recent experiments, which have already been discussed on p. 304, have shown it to be 2:4-*dichlorocamphane* (III), the formation of which involves an isomerisation of the Nametkin type.

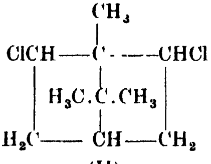
---

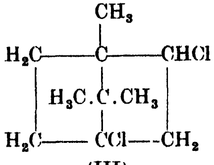
* *Traité*, III, 694.

† *Inter al.*, Spitzer, *Annalen*, 1879, **196**, 262; 1880, **200**, 361; Marsh and Gardner, *J.C.S.* 1897, **71**, 290; Marsh and Hartridge, *ibid.* 1898, **73**, 852; Bredt, *Annalen*, 1900, **314**, 369.

‡ *Annalen*, 1923, **435**, 190.


(I)


(II)


(III)

In 1883 Naegeli[*] observed that camphor reacted readily with hydroxylamine to yield an oxime and thus conclusively proved the presence of the carbonyl group. *d-Camphoroxime*, which can be conveniently prepared by the method used by Auwers,[†] melts at 119°, $[\alpha]_D$ $-42{\cdot}40°$, whilst the enantiomorph prepared from *l*-camphor has $[\alpha]_D$ $+41{\cdot}7°$.[‡] *dl*-Camphoroxime, m.p. 118°, was resolved by Pope by the use of camphor-ω-sulphonic acid. The absorption spectrum in the ultra-violet was studied by Baly, Marsden and Stewart.[§] Camphoroxime, owing to its tendency to pass into α-campholenonitrile (see below), can only with difficulty be reconverted into camphor. The hydrolysis was first effected by Forster,[||] who, by the action of potassium permanganate on the oxime in acid solution, obtained an unstable green substance, which on reduction with zinc dust gave camphor; the hydrolysis can, however, be more readily carried out by the method used by Lapworth,[¶] who heated camphoroxime with a mixture of formaldehyde and hydrochloric acid. Even under these conditions conversion into the nitrile occurs. A large number of derivatives of camphoroxime have been prepared by Forster,[**] but these do not require special comment.

On reduction with sodium in alcoholic or more readily in amyl alcoholic solution, camphoroxime yields a mixture of isomeric bases, *bornylamine* (IV) and neo*bornylamine* (V).[*] These bases are obtained also when camphoroxime is reduced electrolytically[†] by the hydrogenation of camphorimine[‡] and by heating camphor with ammonium formate or formamide, followed by hydrolysis of the formyl derivative so obtained.[§] The separation of the two bases can be readily effected by taking advantage of the sparing solubility of the hydrochloride of the former base.[‖] Bornylamine

---

[*] *Ber.* 1883, **16**, 497.

[†] *Ibid.* 1889, **22**, 605.

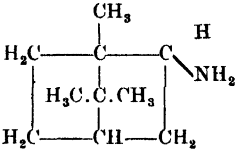
[‡] Pope, *J.C.S.* 1899, **75**, 1109.

[§] *J.C.S.* 1906, **89**, 980.

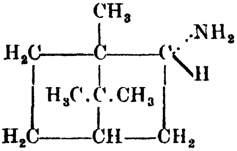
[||] *Ibid.* 1897, **71**, 199.

[¶] *Ibid.* 1907, **91**, 1133.

[**] *Ibid.* 1897, **71**, 191, 1033.



(IV)



(V)

melts at 163°, $[\alpha]_D$ +45·5°, −50·8°, and it has been characterised by the preparation of a large number of derivatives.[¶] *neo*Bornylamine is somewhat difficult to obtain pure. It was purified by Forster by conversion into the sparingly soluble *di*neo*bornyloxamide*, which is formed when the base is heated with ethyl oxalate, but the purification is probably best carried out by using either *d*-hydroxymethylenecamphor, the use of which was first suggested by Pope and Read[**] (compare p. 462), or *l*-abietic acid, which has been recommended by Krestinski and Bardischev.[††] *neo*Bornylamine has m.p. 186°, $[\alpha]_D$ +47·3°, −43·7°. It is somewhat more readily soluble than bornylamine. When treated with nitrous acid or heated with acetic anhydride at 200° under pressure, both bases yield camphene.[‡‡] The conversion of trimethylbornylammonium hydroxide into bornylene is referred to on p. 325. When camphoroxime is reduced by the Sabatier-Senderens process using a nickel catalyst at 180–200°, it yields a mixture of bornylamine, dibornylamine and camphylamine,[*] though according to Alder and Stein[†] hydrogenation under milder conditions gives mainly *neo*bornylamine. Vavon and Chilouet[‡] consider that *neo*bornylamine corresponds in configuration to *iso*borneol.

---

[*] Leukart and Bach, *Ber.* 1887, **20**, 111; Forster, *J.C.S.* 1898, **73**, 370; Konovalov, *J. Russ. Phys. Chem. Soc.* 1901, **33**, 46.

[†] Tafel and Pfeffermann, *Ber.* 1902, **35**, 1515.

[‡] Vavon and Chilouet, *Compt. rend.* 1937, **204**, 53.

[§] Leukart and Bach, *Ber.* 1887, **20**, 104; Wallach and Griepenkerl, *Annalen*, 1892, **269**, 347; Forster, *J.C.S.* 1898, **73**, 386; Ingersoll, Brown, Kim, Beauchamp and Jennings, *J. Amer. C.S.* 1936, **58**, 1810; compare Wegler and Frank, *Ber.* 1936, **69**, 2071.

[‖] Compare Goodson, *J.C.S.* 1927, p. 930.

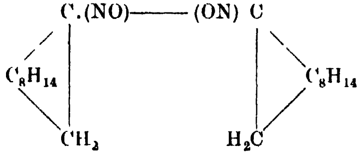
[¶] Forster, *J.C.S.* 1899, **75**, 941; Forster and Hart-Smith, *ibid.* 1900, **77**, 1155; Forster and Attwell, *ibid.* 1904, **85**, 1195; Heubaum and Noyes, *J. Amer. C.S.* 1930, **52**, 5070.

[**] *J.C.S.* 1913, **103**, 458.

[††] *J. Gen. Chem. Russ.* 1940, **10**, 1894.

[‡‡] Compare Hückel and Nerdel, *Annalen*, 1937, **528**, 57.

On oxidation with dilute nitric acid, camphoroxime yields a mixture of camphoric and *iso*camphoronic acids,[§] whilst with more dilute acid pernitrosocamphor (p. 441) is obtained. Oxidation in alkaline solution with potassium permanganate yields camphoric acid, but in acid solution, in addition to this acid, an unstable green nitrogenous substance is obtained, which gives on reduction camphor. According to Rimini,[||] by the action of potassium ferricyanide in alkaline solution a dimolecular *nitroso*-derivative, m.p. 103–105°, is formed, which he suggested has the formula (VI).



(VI)

Forster[¶] found that when camphoroxime was treated with potassium hypochlorite or hypobromite it underwent an interesting reaction yielding *2-chloro-2-nitrocamphane*, m p. 217°, or *2-bromo-2-nitrocamphane* (VII), m.p. 220°, depending upon which reagent was used. When either of these substances is treated with alcoholic potassium hydroxide, *2-nitrocamphane* (VIII), m.p. 147–148°, $[\alpha]_D$ +20·4°, is obtained. The *pseudo*-form (IX), m.p. 74°, $[\alpha]_D$ −94·9°, can be prepared by the careful acidification of the potassium salt. Like those of α-chloro- and α-nitro-camphors, alcoholic solutions of *pseudo*-nitrocamphane show mutarotation.

If 2-bromo-2-nitrocamphane is digested with aqueous sodium hydroxide solution a *nitrile* is obtained, which gives on prolonged

---

[*] Aloy and Brustier, *Bull. Soc. chim.* 1911 [iv], **9**, 733.

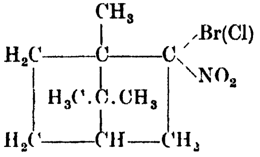
[†] *Annalen*, 1936, **525**, 221.

[‡] *Compt. rend.* 1937, **204**, 53.

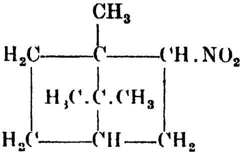
[§] Koenigs, *Ber.* 1893, **26**, 2340; Forster, *J.C.S.* 1897, **71**, 197.

[||] *Gazzetta*, 1896, **26**, ii, 513.

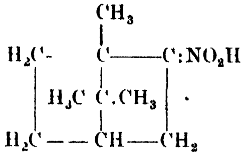
[¶] *J.C.S.* 1899, **75**, 1144; 1900, **77**, 263, compare Ginnings and Noyes, *J. Amer. C.S.* 1922, **46**, 2567.



(VII)

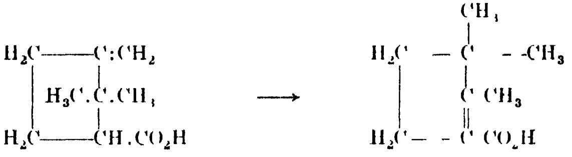


(VIII)



(IX)

boiling with alkali an *amide*, m.p. 90°, and finally an *acid*, $C_9H_{14}O_2$, b.p. 239°/758 mm., d^{16° 1·0146. Forster* suggested that this acid, to which he gave the name *infracampholenic acid*, is 1 : 1-*dimethyl-2-methylene*cyclo*pentane-5-carboxylic acid* (X). This structure for the acid has been confirmed by Lewis and Simonsen who found that it gave on ozonolysis formaldehyde and 1 : 1-dimethyl*cyclo*pentan-2-one-5-carboxylic acid. On treatment with bromine in carbon disulphide solution it yields a *tribromide*, m.p. 182°, whilst in chloroform solution a *dibromide*, m.p. 125°, is formed. When the acid is digested with sulphuric acid it is converted into iso*lauronolic acid* (XI).



(X) (XI)

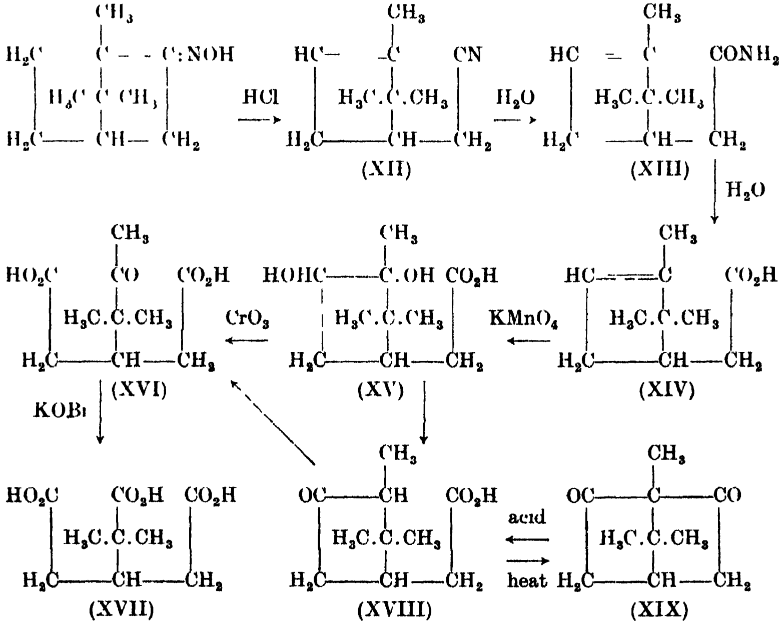
The conversion of 2-bromo-2-nitrocamphane into nitrocamphene has been referred to on p. 313.

When camphoroxime is digested with mineral acids or with acid chlorides, it undergoes a Beckmann transformation and, depending upon the conditions which are used, yields either α-campholenonitrile, α-campholenamide, α-campholenic acid, dihydro-β-campholenolactone, dihydro-β-campholenoiminolactone (compare p. 418), β-campholenamide or β-campholenic acid.† The constitution of these various substances and the mechanism of their formation has been the subject of much controversy, into which it is unnecessary to enter here. The primary product of the reaction (from *d*-camphoroxime) is undoubtedly d-*α-campholenonitrile* (XII), b.p. 226–227°, $[\alpha]_D$ $+7{\cdot}3°$, which is then converted through the *amide* (XIII), m.p. 130·5°, $[\alpha]_D$ $-4{\cdot}9°$, into d-*α-campholenic acid* (XIV), b.p. 142–144°/10 mm., $d^{19°}$ 0·9920, $n_D^{16°}$ 1·4712, $[\alpha]_D$ $+9{\cdot}37°$. The constitution of this acid has been established by its oxidation, either with potassium permanganate in alkaline solution* or by chromic acid,† to d-*dihydroxydihydro-α-campholenic acid* (XV), m.p. 144°, $[\alpha]_D$ $+58{\cdot}2°$, which gives on further oxidation with chromic acid iso*ketocamphoric acid* (XVI), m.p. 129–130°, from which, by the action of potassium hypobromite, *iso*camphoronic acid (XVII) is obtained. On treatment with acids, the dihydroxy-compound (XV) undergoes ketonisation to give *α-campholonic acid* (XVIII), m.p. 65–66°,‡ which on heating passes into 6-*ketocamphor* (XIX) from which it is regenerated by acid hydrolysis.§ The reactions involved are shown in the scheme below:

---

* *J.C.S.* 1901, **79**, 108.

† *Inter al.*, Naegeli, *Ber.* 1884, **17**, 805; Goldschmidt and Schmidt, *ibid.* 2071; Tiemann, *ibid.* 1896, **29**, 3007; 1897, **30**, 243, 328; Béhal, *Bull. Soc. chim.* 1895 [iii], **13**, 837; Konovalov, *J. Russ. Phys. Chem. Soc.* 1901, **33**, 46.



---

* Tiemann and Semmler, *Ber.* 1896, **29**, 529, 3014; Tiemann, *ibid.* 3023.

† Thiel, *ibid.* 1893, **26**, 922.

‡ This was originally thought to be pinonic acid (see p. 120).

§ Miyake and Watanabe, *Proc. Imp. Acad. Tokyo*, 1935, **11**, 106, 322; Komppa and Beckmann, *Ber.* 1936, **69**, 2783.

Although α-campholenic acid is formed to a small extent by the direct action of acids on camphoroxime, it is best prepared by the hydrolysis of the nitrile with alkali. Attention has already been directed to the tendency for ω-substituted derivatives of camphor to pass into this acid. When α-campholenic acid is heated with mineral acids it is converted into dihydro-β-campholenolactone, the reaction being quantitative if hydriodic acid is used, the parent hydroxy acid being obtained if the acid is digested with alkali.[*] This lactone is a derivative of β-campholenic acid and its constitution is discussed on p. 440. If α-campholenic acid is boiled for some time, elimination of carbon dioxide occurs with the formation of the hydrocarbon, *campholene* (p. 440). According to Ingold and Chandrasena,[†] α-campholenic acid is converted into camphor when it is treated with silver oxide in acetone solution, *α-keto-α-campholenic acid* being formed simultaneously. This reaction, for which there is no apparent analogy, is so remarkable that a confirmation would appear desirable. Contamination of the acid with camphor, formed by direct hydrolysis of the oxime, provides a possible explanation. The reduction of α-campholenic acid to the corresponding saturated acid, *campholanic acid*, and the identity of this with *iso*campholic acid, is referred to on p. 444.

When α-campholenonitrile is heated with mineral acids it is isomerised to *β-campholenonitrile*, which can, however, be prepared more conveniently by the action of hydriodic acid on camphoroxime.[‡] The nitrile is an oil, b.p. 225°, $d^{20°}$ 0·9093, $n_D^{20°}$ 1·4704, and it is optically inactive. On hydrolysis with alkalis it yields the corresponding *amide*, m.p. 86°, which can be prepared also by the action of acids on α-campholenamide, and finally the acid, *β-campholenic acid*, m.p. 52°, b.p. 185°/120 mm. This acid is formed also, together with α-campholenic acid, by the action of sodium amalgam on αω-dibromocamphor.[§] β-Campholenic acid is not a true derivative of camphor, a rearrangement of the methyl groups accompanied by a shift of the ethylenic linkage having occurred during the isomerisation. There can be no doubt that it is correctly represented by (XX), since on oxidation with potassium permanganate it yields *dihydroxy-β-campholenic acid* (XXI), of which two isomeric forms, m.p. 146° and 91°, are known. This acid on further oxidation with chromic acid yields the *keto-acid* (XXII), *αα-dimethylglutaric acid* (XXIII) and oxalic acid.

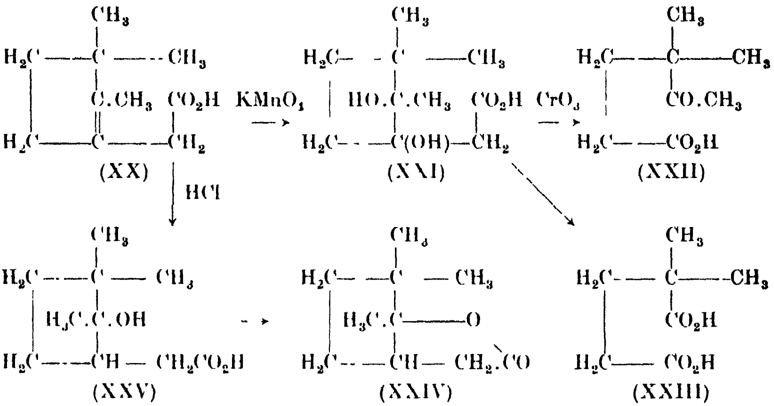
---

[*] Tiemann, *Ber.* 1897, **30**, 405.

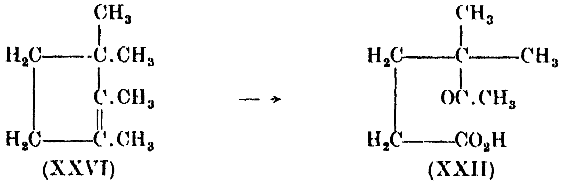
[†] *J.C.S.* 1922, **121**, 1552.

[‡] Tiemann, *Ber.* 1895, **28**, 1083; 1897, **30**, 243.

[§] Kachler and Spitzer, *Monatsh.* 1882, **3**, 216; *Ber.* 1884, **17**, 2400; Tiemann, *Ber.* 1896, **29**, 3010.



When β-campholenic acid is warmed with mineral acids it passes readily into the *lactone* (XXIV) of *hydroxydihydro-β-campholenic acid* (XXV), which as mentioned above can be prepared also from α-campholenic acid.[*] The elimination of carbon dioxide from β-campholenic acid proceeds with greater facility than in the case of the α-isomeride and yields the hydrocarbon, *campholene*, b.p. 134°/758 mm., $d^{20°}$ 0·8034, $n_D^{20°}$ 1·4466.[†] There can be no doubt that this hydrocarbon must be represented by formula (XXVI), since it gives on oxidation (XXII).



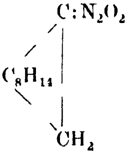
Treatment of camphoroxime in either acetic acid or hydrochloric acid solution with sodium nitrite yields *pernitroso-*

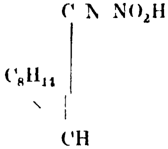
---

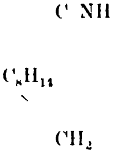
[*] Tiemann, *Ber.* 1895, **28**, 2170; 1897, **30**, 405.

[†] Béhal, *Bull. Soc. chim.* 1895 [iii], **13**, 844; Tiemann, *Ber.* 1895, **28**, 2184.

camphor.[*] This substance can be prepared also by the action of nitrosyl chloride on a chloroform solution of the oxime or its sodium salt,[†] by treatment of the oxime with nitrogen dioxide[‡] or by the action of nitrous acid on its ethereal solution.[§] Two forms of pernitrosocamphor have been prepared, a stable modification (XXVII), m.p. 43°, and an unstable *pseudo*-form (XXVIII), m.p. 65–70°. The latter is obtained when a solution of the stable modification in dilute alkali is carefully acidified.[‖]


(XXVII)


(XXVIII)


(XXIX)

When heated to 150° it gives campholenonitrile.[¶] Like pernitrosofenchone (p. 516), pernitrosocamphor gives on treatment with concentrated sulphuric acid *iso*camphor, 1-methyl-3-*iso*-propyl-Δ^1-*cyclo*hexen-6-one. On reduction with aluminium amalgam a mixture of bornylamine and *neo*bornylamine is formed, whilst ammonia converts it into *camphorimine* (XXIX), m.p. 95°. This substance, which is extremely poisonous,[**] is the primary product of the action of nitrous acid on camphoroxime and can be separated from pernitrosocamphor by taking advantage of the sparing solubility of its nitrate. On hydrogenation over platinum it gives *neo*bornylamine.[††] By the action of hydrogen cyanide on camphorimine Houben and Pfankuch[‡‡] obtained a nitrile, m.p. 170–171°, which by the action of nitrous acid gave a substance, m.p. 159°, which they suggested was *camphorcyanohydrin.* An isomeric camphorcyanohydrin, m.p. 209°, was prepared by the action of hydrogen cyanide on pernitrosocamphor. Lapworth, Manske and Robinson[§§] pointed out the extreme improbability that either of these substances could be camphorcyanohydrin, and the more recent experiments of Houben and Pfankuch* have shown this criticism to be justified. The cyanohydrin, m.p. 159°, has been shown to be represented by (XXX), since it can be converted through the *ketone* (XXXI) into *camphenic acid* (XXXII). The isomeric "cyanohydrin", m.p. 209°, has been found to be the *amide* of *camphene-1-carboxylic acid* (XXXIII); when treated with hydrogen chloride it undergoes both the Nametkin and Wagner changes, to give *2-chlorocamphane-4-carboxylamide* (XXXIV), m.p. 128°, which with potassium carbonate gives the *amide* of *camphene-4-carboxylic acid* (XXXV), m.p. 164–165°.

---

[*] Angeli and Rimini, *Ber.* 1895, **28**, 1078; *Gazzetta*, 1899, **29**, ii, 36.

[†] Angelucci, *Annalen*, 1905, **341**, 180.

[‡] Forster, *J.C.S.* 1897, **71**, 198.

[§] Tiemann, *Ber.* 1895, **28**, 1080; Mahla and Tiemann, *ibid.* 1896, **29**, 2807.

[‖] Hantzsch and Dollfus, *ibid.* 1902, **35**, 260.

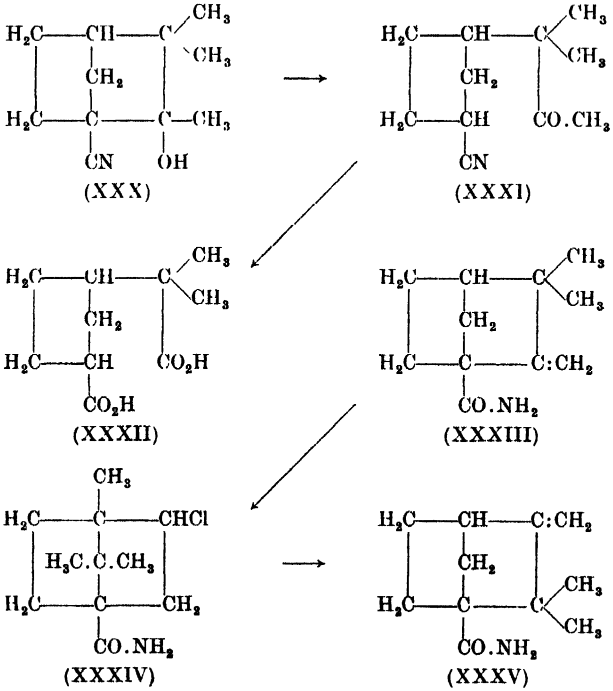
[¶] Gandini, *Gazzetta*, 1942, **72**, 131.

[**] Merling, *Ber.* 1896, **29**, 2808.

[††] Vavon and Chilouet, *Compt. rend.* 1937, **204**, 53.

[‡‡] *Ber.* 1927, **60**, 586; compare Passerini, *ibid.* p. 1201; Gandini, *Gazzetta*, 1939, **69**, 190.

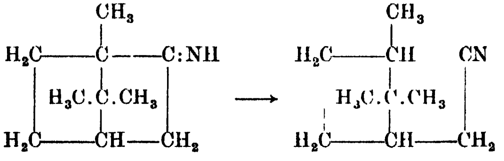
[§§] *J.C.S.* 1927, p. 2052.

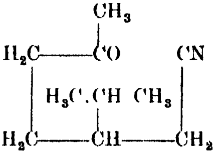


When camphorimine (XXIX) is heated in a current of air at 100°, ring fission occurs with the formation of a *nitrile*, $C_{10}H_{17}N$, and β-iso*propyl-δ-acetylvaleronitrile* (XXXVI).* The former nitrile was considered to be that of dihydro-α-campholenic acid and was represented by formula (XXXVII), although no direct evidence of its structure was obtained. On hydrolysis of the nitrile a liquid acid, b.p. 160°/22 mm., $[\alpha]_D$ +28·26°, was obtained, from which an *amide*, m.p. 143°, $[\alpha]_D$ +2·5°, was prepared. If this acid has been correctly formulated, it should be identical with one of the acids having this composition obtained by Guerbet† by the fusion of camphor with potassium hydroxide.

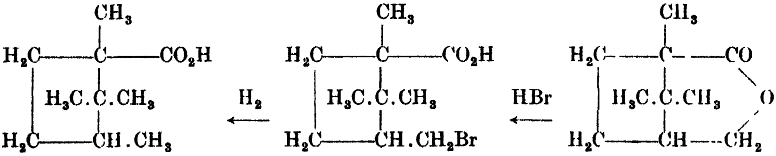
---

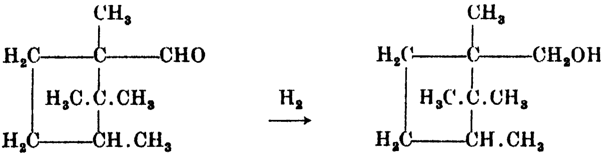
* *Annalen*, 1930, **483**, 271; 1931, **489**, 193.


(XXIX) (XXXVII)


(XXXVI)

When camphor is fused with potassium hydroxide it yields two acids, generally known as campholic and *iso*campholic acids, the former being obtained in larger amount. These acids, the latter of which is an oil, have long been known, since the former was isolated in 1841 by Delalande‡ as a product of the distillation of camphor over potassium hydroxide. *Campholic acid*, *d*- and *l*-, m.p. 106–107°, *amide*, m.p. 79–80°, *dl*-, m.p. 109°, *amide*, m.p. 90°, is undoubtedly represented by formula (XXXVIII), since it


(XXXVIII) (XXXIX) (XL)


(XLI) (XLII)

---

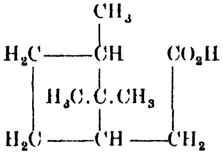
* Mahla and Tiemann, *Ber.* 1900, **33**, 1930.

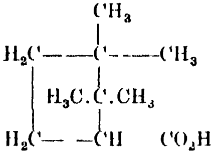
† *Bull. Soc. chim.* 1894 [iii], **12**, 905; 1895 [iii], **13**, 769; 1910 [iv], **7**, 68.

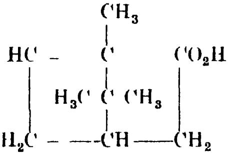
‡ *Ann. Chim.* 1841 [iii], **1**, 120.

yields on oxidation with nitric acid a mixture of camphoric and camphoronic acids. This constitution has been confirmed by its synthesis by Haller and Blanc* by the reduction of *bromo-d-campholic acid* (XXXIX) prepared by the action of hydrogen bromide on α-*campholide* (XL). *Campholaldehyde* (XLI) prepared from the phenylimidochloride of campholic acid, on hydrogenation gives *campholcarbinol* (XLII), m.p. 60°.†

Much greater difficulty has been met with in determining the constitution of *iso*campholic acid. From its method of formation it may be either stereoisomeric with campholic acid, or represented by either formula (XLIII) or (XLIV). If the former be the correct representation, then *iso*campholic acid should be identical with Mahla and Tiemann's dihydro-α-campholenic acid, and also with the acid prepared by the reduction of α-campholenic acid (XIV). The reduction of α-campholenic acid was unsuccessfully attempted by Béhal,‡ but has been achieved by Kregten§ and by Lipp.‖ By the reduction of *dl*-α-campholenic acid (from *dl*-camphoroxime) with hydrogen in the presence of platinum black, Lipp prepared dl-cis-*campholanic acid*, b.p. 150·9–151·2°/14 mm., which gives an *amide*, m.p. 129–130°, the amide of the corresponding *d*-acid melting at 150°. By the reduction of α-campholenamide he prepared the *amide* of dl-trans-*campholanic acid*¶ and this melted at 124·5–125°. This latter amide was found to be identical with the amide of *dl*-dihydro-α-campholenic acid prepared by Mahla and Tiemann's method from camphoroxime. Proof was thus obtained that


(XLIII)


(XLIV)


(XIV)

---

* *Compt. rend.* 1900, **130**, 376.

† v. Braun and Manz, *Ber.* 1934, **67**, 1700.

‡ *Bull. Soc. chim.* 1895 [iii], **13**, 846; 1904 [iii], **31**, 179.

§ *Rec. trav. chim.* 1916, **36**, 64.

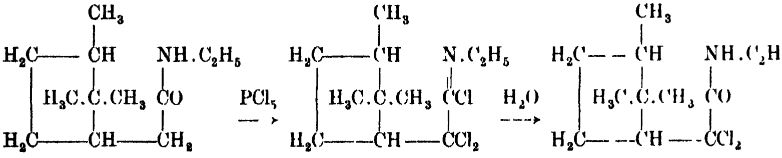
‖ *Ber.* 1922, **55**, 1883.

¶ *trans*-Campholanic acid has also been prepared by Komppa (*Ber.* 1936, **69**, 2783) by reduction of the semicarbazone of α-campholonic acid (p. 438) with sodium ethoxide.

dihydro-α-campholenic and *trans*-campholanic acids were identical, but Lipp was less successful in his attempt to establish the identity of *iso*campholic acid and either *cis*- or *trans*-campholanic acids. Their identity has, however, been established by the ingenious experiments of v. Braun and Heymons.* It had been observed by v. Braun that, when the amides or alkyl amides of acids which had the carboxyl group attached to a tertiary carbon atom were treated with phosphorus pentachloride, a chloroimide was formed, from which the original acid could be regenerated by the action of water. If, however, the acid contained a $>CH$- or —CH_2-group in the α-position to the carboxyl group, then, on treatment with phosphorus pentachloride, a di- or trichloride was obtained, which with water gave a chloro- or dichloroamide. The reactions are indicated by the scheme:

$$\begin{array}{llll}
CR_3.CONHR & \xrightarrow{PCl_5} CR_3.C(Cl){:}NR & \xrightarrow{H_2O} & CR_3.CONHR \\
CHR_2.CONHR & \longrightarrow CR_2Cl.C(Cl){:}NR & \longrightarrow & CR_2Cl.CONHR \\
CH_2R.CONHR & \longrightarrow CRCl_2.C(Cl){:}NR & \longrightarrow & CRCl_2.CONHR
\end{array}$$

On applying this reaction to iso*campholethylamide* (XLV), m.p. 41–42°, a *dichloroimidochloride* (XLVI), b.p. 145–150°/15 mm., was obtained, which on treatment with water gave *dichloro*iso*campholethylamide* (XLVII), m.p. 73–77°, b.p. 125–127°/0·2 mm. There can therefore be no doubt that *iso*campholic acid is identical with campholanic acid, and that Lipp's failure to establish the identity was due to the difficulty encountered in purifying *iso*campholic acid.



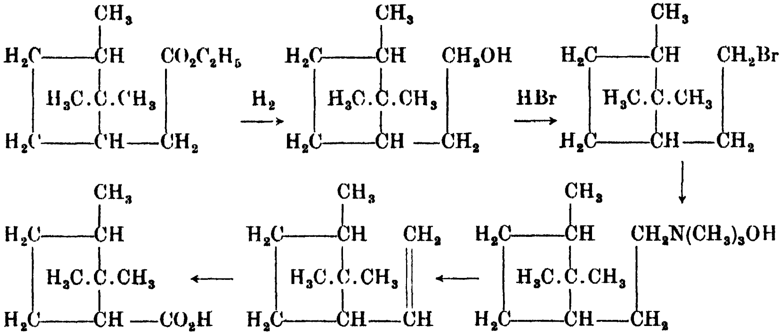
(XLV) (XLVI) (XLVII)

Additional proof of the presence of the group —$CH_2.CO_2H$ in *iso*campholic acid was furnished by its conversion into *nor*iso*campholic acid*, 2:2:3-*trimethyl*cyclo*pentanecarboxylic acid*

---

* *Ber.* 1928, **61**, 2276; compare Rupe and Briellmann, *Helv. Chim. Acta*, 1922, **5**, 767.

(XLVIII), b.p. 130°/12 mm., *ethylimide*, m.p. 68–69°, by the reactions shown in the scheme:



(XLVIII)

Camphorhydrazone, which can be readily prepared by the action of hydrazine on the ketone, melts at 55° and the *azine*, which is formed simultaneously, melts at 182°. The conversion of the hydrazone into camphane has been referred to on p. 273. Camphorhydrazone has also been prepared by heating camphorquinonemonohydrazone with hydrazine hydrate at 150°.[*]

Camphoranil, m.p. 13·5°, b.p. 166°/15 mm., is obtained by the condensation of camphor with aniline[†] and by the dehydrogenation of *iso*bornylaniline with sulphur;[‡] it is readily hydrolysed to camphor and aniline.

Thiocamphor, *l*-, m.p. 146°, $[\alpha]_D^{30^\circ}$ -12° (in alcohol); *dl*-, m.p. 145°, is prepared by the treatment of camphor with hydrogen sulphide in the presence of hydrochloric acid. On reduction with zinc and hydrochloric acid it gives *thioborneol*, m.p. 120°.[§]

As a general rule camphor reacts normally with the Grignard reagent; thus with methyl magnesium iodide methylborneol is obtained.[‖] The products of the dehydration of this alcohol are discussed on p. 579. With propyl magnesium bromide, camphor is reduced to borneol and *iso*borneol,[*] although with allyl bromide or iodide allylborneol can be prepared.[†]

---

[*] Forster and Kunz, *J.C.S.* 1914, **105**, 1721.

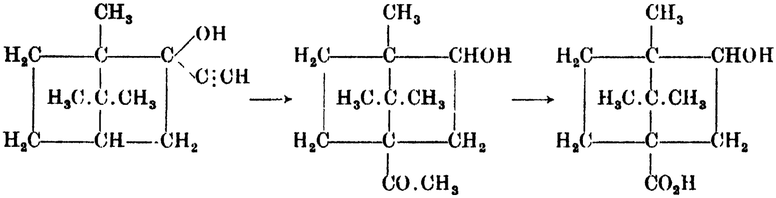
[†] Reddelien and Meyn, *Ber.* 1920, **53**, 352.

[‡] Ritter, *J. Amer. C.S.* 1933, **55**, 3322.

[§] Sen, *J. Ind. C.S.* 1935, **12**, 647, 751; 1936, **13**, 523; 1937, **14**, 214; 1938, **15**, 537.

[‖] Zelinski, *Ber.* 1901, **34**, 2883; Wallach and Wienhaus, *Annalen*, 1907, **353**, 224; Ruzicka, *Helv. Chim. Acta*, 1918, **1**, 110; Bredt and Savelsberg, *J. pr. Chem.* 1918 [ii], **98**, 97; Bredt-Savelsberg and Buchkremer, *Ber.* 1931, **64**, 600.

Camphor reacts with sodium acetylide to give *ethynylbornyl alcohol* (XLIX), m.p. 97–98°, which on heating with formic acid undergoes hydration and rearrangement to give a product, m.p. 77–78°, formulated by Hurd and Christ[‡] as 2-acetyl-6-hydroxycamphane, but which is more probably 4-*acetylborneol* (L), formed by a Nametkin isomerisation, since on oxidation it gives *borneol-4-carboxylic acid* (LI), m.p. 221°.[§]



(XLIX) (L) (LI)

SOME REACTIONS OF CAMPHOR INVOLVING THE α-CARBON ATOM

The —CH_2-group adjacent to the carbonyl group in camphor is extremely reactive and it will be convenient to consider together some of the diverse reactions in which it is involved.

Although there can be no doubt that camphor reacts with sodium in its enolic form (I), and the existence of this tautomeride in solution is confirmed by the action of the Grignard reagent,[||] the only derivative known would appear to be the ethyl ether (III). *Camphor-enol ethyl ether* or 2-*ethoxybornylene* was prepared by Bredt-Savelsberg and Rumscheidt[¶] from camphoracetal (II), b.p. 102–103°/11·5 mm.,[**] by the action of phosphorus pentoxide in pyridine solution. It is an oil, b.p. 73·9–75·1°/12 mm., $d_{4°}^{10·8°}$ 0·9536, $n_D^{10·3°}$ 1·4679, and gives on oxidation with potassium permanganate *β-ethyl hydrogen camphorate* (IV). It is extremely unstable and is readily hydrolysed to camphor by water or dilute acids.

---

[*] Leroide, *Ann. Chim.* 1921 [ix], **16**, 365.

[†] Chojn, *J. Russ. Phys. Chem. Soc.* 1912, **44**, 1844; compare Nametkin and Schavrigin, *Ber.* 1933, **66**, 511.

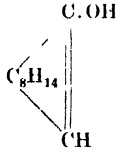
[‡] *J. Amer. C.S.* 1937, **59**, 118; compare Dulou, *Bull. Inst. Pin*, 1934, **178**, 197.

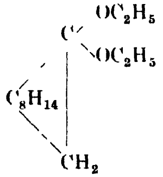
[§] Hurd and Christ incorrectly describe this acid as borneol-6-carboxylic acid (compare Houben and Pfankuch, *Annalen*, 1931, **489**, 193).

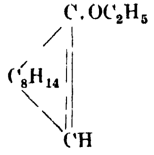
[||] Bredt-Savelsberg, *J. pr. Chem.* 1924 [ii], **107**, 65.

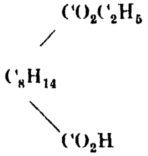
[¶] *Ibid.* 1927 [ii], **115**, 235.

[**] Compare Arbusov, *J. Russ. Phys. Chem. Soc.* 1908, **40**, 637.


(I)


(II)


(III)


(IV)

A large number of derivatives of camphor have been prepared by taking advantage of the reactivity of *sodiocamphor*. It will not be possible to discuss all these in detail and only the more important reactions will be referred to. Sodiocamphor is obtained when camphor is allowed to react with sodium in any neutral solvent (ether, benzene, etc.). When prepared in this manner it is always contaminated with the sodium derivatives of borneol and *iso*borneol, owing to partial reduction of the ketone during the preparation of the sodium compound. It can be obtained in a higher state of purity by the use of sodamide in place of sodium.[*] When sodiocamphor is heated in toluene solution it yields a mixture of campholic and *iso*campholic acids, bornylcamphor, and bornylenecamphor,[†] whilst by the action of iodine α-iodocamphor is obtained.[‡] It has also been shown by Morgan and his collaborators[§] that it can be used for the preparation of arsenic, antimony and phosphorus derivatives of camphor.

In 1870 Baubigny[||] observed that when carbon dioxide was allowed to react with sodiocamphor in toluene an acid was formed. This acid was prepared subsequently by Kachler and Spitzer[¶] by the action of sodium and carbon dioxide on αα′-dibromocamphor, and by Oddo[**] in a similar manner from α-bromocamphor, whilst Haller[††] obtained it by the hydrolysis of α-cyanocamphor (p. 454). *Camphor-3-carboxylic acid* (V) can also be obtained by the Grignard reaction from α-bromocamphor,[*] but it is best prepared from sodiocamphor by the action of carbon dioxide under the conditions described by Bredt and Sandkuhl.[†] A partial synthesis of camphor-3-carboxylic acid has been achieved by Ruzicka,[‡] who prepared ethyl camphor-3-carboxylate by the action of sodium ethoxide on ethyl homocamphorate. This synthesis is of interest, since homocamphoric acid can be very readily obtained by heating camphor-3-carboxylic acid with sodium ethoxide at 200° in an autoclave.[§] The *d*- and *l*-acids melt at 127–128°, $[\alpha]_D \pm 18°$; decomposition occurs at the melting-point with evolution of carbon dioxide, and camphor is regenerated. In aqueous solution the acid gives with ferric chloride a blue coloration, which on standing becomes green. When oxidised with nitric acid camphoric acid is obtained, whilst with an alkaline solution of potassium permanganate a mixture of this acid and camphorquinone results. Camphor-3-carboxylic acid can be readily chlorinated and brominated, the *chloro*-acid melting at 93–94°[¶] and the *bromo*-acid at 112–113°.[**] Both acids on heating yield the corresponding α-halogenated camphors. Although camphor-3-carboxylic acid itself and its halogen derivatives have only been prepared in one modification, it is of interest to note that Bruhl[††] has obtained *methyl bromocamphor-3-carboxylate* in two modifications, m.p. 53–54° and 60–61°, which are probably represented by the formulae (VI) and (VII).

---

[*] Bruhl, *Ber.* 1903, **36**, 1305; 1904, **37**, 2171.

[†] de Montgolfier, *Ann. Chim.* 1878 [v], **14**, 99; Guerbet, *ibid.* 1895 [vii], **4**, 291; *Bull. Soc. chim.* 1910 [iv], **7**, 69.

[‡] Haller, *Compt. rend.* 1878, **87**, 843; Bruhl, *Ber.* 1904, **37**, 2172.

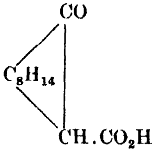
[§] Morgan, Mickelthwait and Whitby, *J.C.S.* 1910, **97**, 34; Morgan and Moore, *ibid.* 1698.

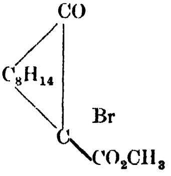
[||] *Ann. Chim.* 1870 [iv], **19**, 221.

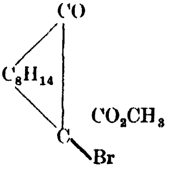
[¶] *Monatsh.* 1881, **2**, 237.

[**] *Gazzetta*, 1893, **23**, I, 74.

[††] *Compt. rend.* 1886, **102**, 1477; compare Minguin, *ibid.* 1891, **112**, 1369.


(V)


(VI)

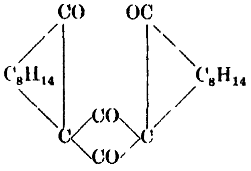

(VII)

---

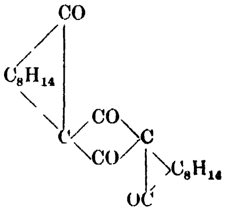
[*] Zelinski, *Ber.* 1903, **36**, 208; Bruhl, *ibid.* p. 668; Malmgren, *ibid.* p. 2622.
[†] *Annalen*, 1909. **366**, 11.
[‡] *Helv. Chim. Acta*, 1920, **3**, 748.
[§] Haller and Minguin, *Compt. rend.* 1890, **110**, 410.
[||] Aschan, *Ber.* 1894, **27**, 1447.
[¶] Schiff and Puliti, *ibid.* 1883, **16**, 887.
[**] de Santos e Silva, *ibid.* 1873, **6**, 1092; Aschan, *ibid.* 1894, **27**, 1445.
[††] *Ibid.* 1902, **35**, 4114.

It does not appear to have been determined whether solutions of camphor-3-carboxylic acid show mutarotation, but this has been observed to occur in the case of solutions of the amide and piperidide, the curves being of considerable complexity.[*] The absorption spectrum of camphor-3-carboxylic acid was studied by Lowry and his collaborators in the course of an elaborate series of investigations.[†] On treatment with nitrous acid camphor-3-carboxylic acid yields *iso*nitrosocamphor (p. 471) and camphorquinone (p. 466).

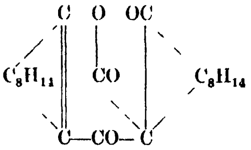
If the acid chloride of bromocamphor-3-carboxylic acid is distilled it yields, according to Staudinger and Schotz,[‡] a mixture of two *cyclo*butane derivatives (VIII) and (VIIIa) melting at 152–153° and 150–151° respectively. On hydrolysis with alkali they yield the parent acid.



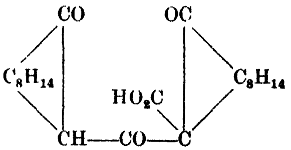
(VIII)



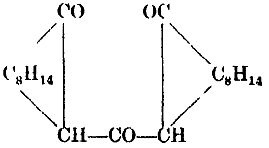
(VIIIa)



(IX)



(X)



(XI)

By the action of acetyl chloride on camphor-3-carboxylic acid Kachler and Spitzer[§] obtained a substance, $C_{22}H_{28}O_4$, m.p. 195–

---

[*] Lowry and Glover, *J.C.S.* 1913, **103**, 913.

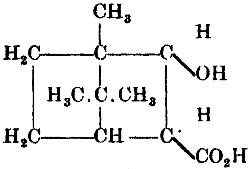
[†] *Ibid.* 1909, **95**, 807, 1340; 1910, **97**, 899, 905.

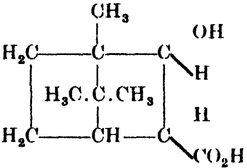
[‡] *Ber.* 1920, **53**, 1105.

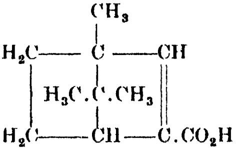
[§] *Monatsh.* 1881, **2**, 241.

196°, which has been found by Staudinger and Schotz[*] to be formed also when the acid chloride of camphor-3-carboxylic acid is distilled. This substance is probably represented by formula (IX), and when shaken with hydrochloric acid it gives the acid (X), m.p. 262°. The latter on warming with alkali yields the triketone (XI).

Although camphor-3-carboxylic acid cannot be reduced to the corresponding hydroxy acid by sodium in alcoholic solution or by any of the ordinary methods, electrolytic reduction proceeds smoothly if a potassium amalgam cathode be used. Two stereoisomeric borneol-3-carboxylic acids are thus obtained and have been studied in great detail by Bredt and his collaborators.[†] cis-iso*Borneol-3-carboxylic acid* (XII) melts at 101° (*dl*-, m.p. 130–132°) and the *trans*-acid (XIII) at 171° (*dl*-, m.p. 145°), the former being converted into the latter on warming with acetyl chloride. A third stereoisomeride, dl-trans-iso*borneol-3-carboxylic acid*, m.p. 169° (*acetyl* derivative, m.p. 116°) has been obtained by indirect means (see p. 452). All these acids yield on dehydration the same *bornylenecarboxylic acid* (XIV), m.p. 112–113°, (*dl*-, m.p. 110–112°), the conversion of which into bornylene has been referred to on p. 324. This acid must have the constitution assigned to it, since it gives on reduction camphane-3-carboxylic acid. The preparation of epicamphor from bornylenecarboxylic acid will be described on p. 514. It was mentioned in discussing the conversion of bornylenecarboxylic acid into bornylene (p. 325, footnote), that, when the acid was treated with hydrogen bromide in acetic acid solution, it gave the normal β-bromide (XV), whilst in aqueous solution an isomeric bromide was obtained. The normal bromide, on warming its sodium salt, gives, in addition


(XII)


(XIII)

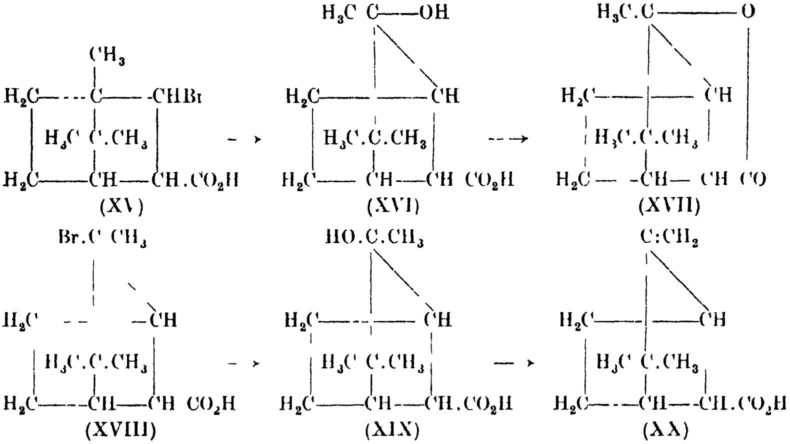

(XIV)

---

[*] *Ber.* 1920, **53**, 1105.

[†] Bredt and Burkheim, *Annalen*, 1906, **348**, 199; Bredt and Sandkuhl, *J. pr. Chem.* 1931 [ii], **131**, 132.

to bornylene and bornylenecarboxylic acid, the *lactone* (XVII), which is derived from the cis-*hydroxy* acid (XVI).



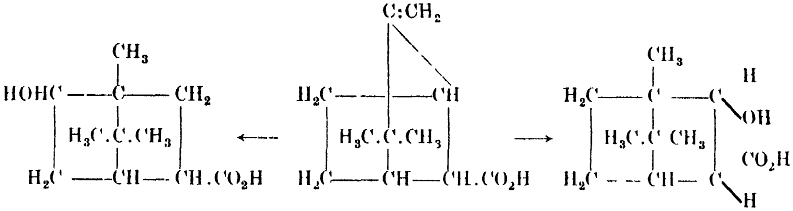
The formation of the isomeric *bromo-acid*, m.p. 157°, by the action of aqueous hydrogen bromide involves a Wagner rearrangement, since this acid is represented by the formula (XVIII). It yields on treatment with sodium carbonate the trans-*hydroxy acid* (XIX), m.p. 176°, which gives on dehydration *camphene-7-carboxylic acid* (XX), m.p. 76–77°. This acid can be prepared also by digesting the bromo-acid with quinoline; it shows no tendency to isomerise to bornylenecarboxylic acid. On hydration of camphenecarboxylic acid (XX) a Wagner rearrangement occurs with the formation of *dl-trans-iso*borneol-3-carboxylic acid (XXI) (see p. 453);* this is accompanied by another isomeric acid, m.p. 180–181°, which Bredt considered to be a borneol-5-carboxylic acid (XXII), but its formation cannot be explained by a normal Wagner rearrangement, and an unequivocal proof of its structure would appear to be desirable. If however, this structure is correct, it is possible that the acid may be formed through the intermediate formation of a tricyclene carboxylic acid, although, as pointed out on p. 158, tricyclene itself cannot be an intermediate in the interconversion of camphene and borneol.

Methyl camphor-3-carboxylate, b.p. 142·5–143°/12 mm.,† gives

---

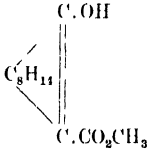
* Bredt, *J. pr. Chem.* 1931 [ii], **131**, 137.

† Bruhl, *Ber.* 1902, **35**, 3515.

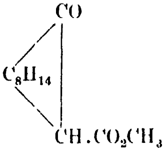


(XXII) (XX) (XXI)

with ferric chloride in alcoholic solution a lilac coloration, and it readily yields a sodium derivative. Like ethyl acetoacetate it can react in both the enolic and ketonic forms (XXIII) and (XXIV), derivatives of both having been prepared.

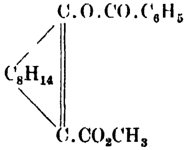


(XXIII)

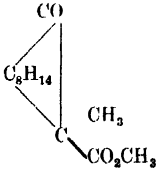


(XXIV)

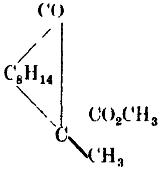
Thus, when the sodium derivative of the ester is treated with benzoyl chloride in light petroleum solution, it yields *methyl O-benzoylcamphor-3-carboxylate* (XXV), m.p. 58–59·5°,* whilst by the action of methyl iodide *methyl 3-methylcamphor-3-carboxylate* can be prepared.† Two forms of this ester have been described, one of which is crystalline, m.p. 87°, $[\alpha]_D$ +17·25 , and the other an oil, b.p. 135–140°/13 mm., $[\alpha]_D$ +75°. These two esters are probably the stereoisomerides (XXVI) and (XXVIa).



(XXV)



(XXVI)



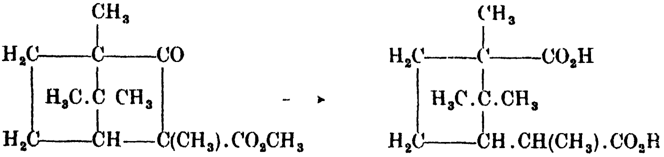
(XXVIa)

By hydrolysis of the crystalline ester the corresponding *acid*, m.p. 104°, has been prepared, which readily loses carbon dioxide with the formation of α-methylcamphor. If the liquid ester is hydrolysed with potassium hydroxide in a sealed tube it yields a mixture of α-methylcamphor and *α-methylhomocamphoric acid* (XXVII), m.p. 143°, $[\alpha]_D$ +38·14°. A stereoisomeric modification of this acid, m.p. 178–180°, $[\alpha]_D$ +26·31°, is obtained by the hydrolysis of α-methyl-α-cyanocamphor (XXXIV) (p. 455).[*]

---

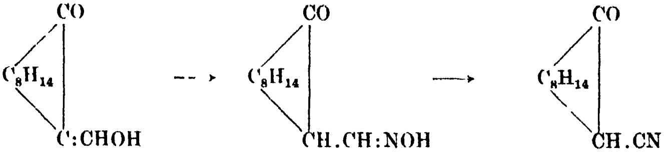
* Brühl, *Ber.* 1903, **36**, 4273.

† Minguin, *Compt. rend.* 1903, **137**, 1067; Brühl, *Ber.* 1902, **35**, 3623.


(XXVI or XXVIa) (XXVII)

A large number of other derivatives of the esters of camphor-3-carboxylic acid have been prepared, but these do not require specific mention.

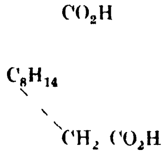
The nitrile of camphor-3-carboxylic acid, α- (or 3-) *cyanocamphor* (XXX), was obtained originally by Haller[†] by the action of cyanogen or cyanogen chloride on sodiocamphor, but, as was shown by Bishop, Claisen and Sinclair,[‡] it can be prepared much more conveniently by the action of hydroxylamine on an alkaline solution of *hydroxymethylenecamphor* (XXVIII), the oxime (XXIX) being an intermediate product of the reaction. It has been shown that the "Camphylisoxazole", prepared by Tingle[§] by the action of hydroxylamine on camphorglyoxylic acid, is identical with α-cyanocamphor.[‖]


(XXVIII) (XXIX) (XXX)

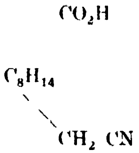
α-Cyanocamphor, which is dimorphous, melts at 127–128°, $[\alpha]_D$ +12·16° (in alcohol); its rotatory power shows very marked variations depending upon the nature of the solvent and the concentration of the solution.[¶] On bromination, preferably with sodium hypobromite, *bromocyanocamphor*, m.p. 74–75°, is obtained, the corresponding *chloride* melting at 98–100°. By prolonged digestion with aqueous sodium hydroxide the cyano-group is hydrolysed, ring fission occurring simultaneously with the formation of homocamphoric acid (XXXI) (Haller), whilst, when warmed for a short time with an alcoholic solution of potassium hydroxide, the corresponding nitrile (XXXII) is obtained.*

---

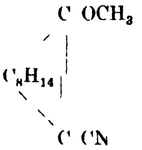
[*] Haller and Minguin, *Compt. rend.* 1894, **118**, 691.
[†] *Ibid.* 1878, **87**, 843.
[‡] *Annalen*, 1894, **281**, 349; compare Lapworth, *J.C.S.* 1900, **77**, 1058.
[§] *Amer. Chem. J.* 1897, **19**, 393.
[‖] Johnson and Shelberg, *J. Amer. C.S.* 1945, **67**, 1745, 1754.
[¶] Haller and Minguin, *Compt. rend.* 1903, **136**, 1527.



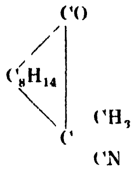
(XXXI)



(XXXII)

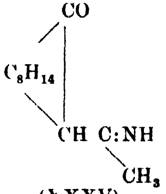


(XXXIII)

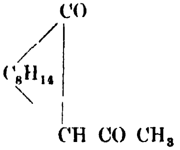


(XXXIV)

Like the esters of camphor-3-carboxylic acid, α-cyanocamphor, which is soluble in alkali, can react both in its enolic and ketonic modifications, and derivatives of both are known. Thus, when the sodium derivative is treated with methyl iodide in alcoholic solution, it yields a mixture of the *O-methyl* derivative (XXXIII), m.p. 63°, $[\alpha]_D$ + 146° (in benzene), and the *C-methyl* derivative (XXXIV), b.p. 170–180°/36 mm., $[\alpha]_D$ + 93·7 (in benzene). The two alkyl derivatives can be readily distinguished, since the former gives on hydrolysis α-cyanocamphor, whilst the latter on prolonged boiling with dilute hydrochloric acid is converted into α-methyl-homocamphoric acid (XXVII) (see above). Forster and Judd† found that α-cyanocamphor reacts readily with methyl magnesium iodide to give the *imine* of acetylcamphor (XXXV), m.p. 126°, which when boiled with dilute hydrochloric acid yields *acetylcamphor* (XXXVI).



(XXXV)



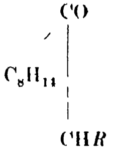
(XXXVI)

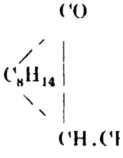
---

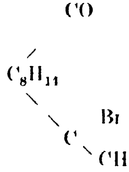
* Minguin, *Ann Chim.* 1893 [vi], **30**, 523; 1894 [vii], **2**, 394.

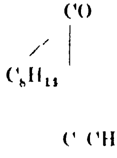
† *J.C.S.* 1905, **87**, 371.

For the preparation of the monoalkyl derivative of camphor having the formula (XXXVII) two general methods are available: (i) treatment of sodiocamphor with alkyl halides and (ii) elimination of carbon dioxide from alkylated camphorcarboxylic acids. In general, the properties of the alkylated camphors resemble those of camphor. Thus *α-methylcamphor* (XXXVIII), which has been prepared by the action of methyl iodide on sodiocamphor* and by the hydrolysis of methyl 3-methylcamphor-3-carboxylate (p. 453),† crystallises in leaflets, m.p. 38°, b.p. 220–221°, $[\alpha]_D$ +30°. It yields on bromination *α′-bromo-α-methylcamphor* (XXXIX), m.p. 62·5 , $[\alpha]_D$ +184·4 , from which, by the action of alkali, *α-methylenecamphor* (XL), m.p. 30–35°, $[\alpha]_D$ +127·5 , can be prepared.

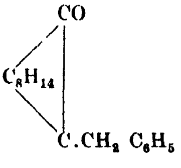

(XXXVII)

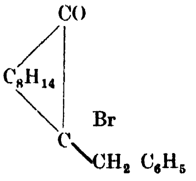

(XXXVIII)

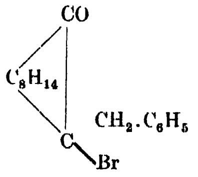

(XXXIX)


(XL)

The monoalkyl derivatives of camphor should exist in two stereoisomeric modifications, corresponding to the α- and α′-forms of chlorocamphor. These do not appear to have been isolated, but from benzylcamphor (XLI) two *bromobenzylcamphors* (XLII) and (XLIIa), m.p. 94–95°, $[\alpha]_D$ +61°, and m.p. 90–91°, $[\alpha]_D$ +20°, have been prepared.‡ These bromides must be stereo- and not structural isomerides, since they both yield benzylidenecamphor (see below) on treatment with alkali.


(XLI)


(XLII)


(XLIIa)

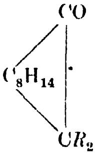
---

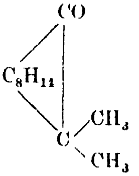
* Haller and Bauer, *Compt. rend.* 1909, **148**, 1645; *Ann. Chim.* 1917 [ix], **8**, 117.

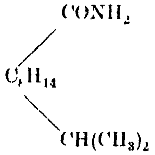
† Minguin, *Ann. Chim.* 1894 [vii], **2**, 284; Bruhl, *Ber.* 1902, **35**, 3624; Glover, *J.C.S.* 1908, **93**, 1291.

‡ Haller and Minguin, *Compt. rend.* 1901, **133**, 80; 1903, **136**, 69.

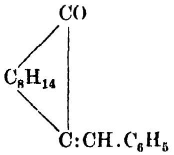
Dialkyl derivatives of camphor (XLIII) can be prepared by the treatment of sodiocamphor or sodioalkylcamphors with alkyl halides. They have been chiefly studied by Haller and his collaborators.[*] *Dimethylcamphor* (XLIV) is an oil, b.p. 106°/11 mm., $[\alpha]_D$ +92·7°. Like fenchone (p. 564), ring fission occurs when the ketone is heated with sodamide in benzene solution with the formation of *dimethylcampholamide* (XLV).

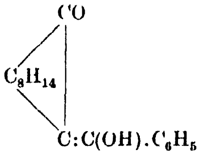

(XLIII)


(XLIV)


(XLV)

A number of alkylidene derivatives of camphor have been described and, as typical of the class, *α-benzylidenecamphor* (XLVI), may be considered. α-Benzylidenecamphor, m.p. 98°, $[\alpha]_D$ +451° (in chloroform), *oxime*, m.p. 197°, was first prepared by Haller[†] by the interaction of sodiocamphor and benzaldehyde, and subsequently[‡] by the action of benzaldehyde on sodioborneol and *iso*borneol. As mentioned above, it was obtained by Haller and Minguin by the action of alkali on the two isomeric bromobenzylcamphors. Of interest also is its preparation by the reduction of the enolic modification of *α-benzoylcamphor* (XLVII) with sodium amalgam.[§] Benzylidenecamphor can be characterised by the preparation of the *nitrosate*, m.p. 188°.[‖] When benzylidenecamphor is heated with hydrogen bromide in acetic


(XLVI)


(XLVII)

---

[*] *Inter al.*, Haller and Bauer, *Ann. Chim.* 1917 [ix], **8**, 117; Haller and Louvrier, *ibid.* 1918 [ix], **9**, 190; compare v. Braun and Kurtz, *Ber.* 1934, **67**, 225; Reinartz and Meesen, *ibid.* 1939, **72**, 1.

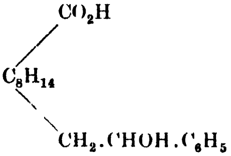
[†] *Compt. rend.* 1891, **113**, 24.

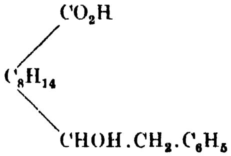
[‡] *Ibid.* 1900, **130**, 689.

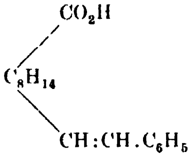
[§] Forster, *J.C.S.* 1903, **83**, 103. For another general method for the preparation of alkylidenecamphors from chloromethylenecamphor, see p. 461.

[‖] Haller, *Compt. rend.* 1895, **121**, 30.

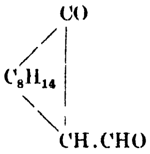
acid solution at 100° ring fission occurs with the formation of *phenylhydroxyhomocampholic acid,* m.p. 206°, which may be represented by either formula (XLVIII) or (XLIX).[*] The latter formula would appear to be the more probable, since on digestion with formic acid *benzylidenecampholic acid* (L), m.p. 124–125°, is obtained.

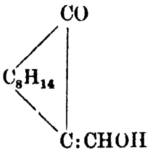

(XLVIII)

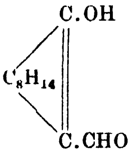

(XLIX)


(L)

By the action of amyl formate on sodiocamphor Bishop, Claisen and Sinclair[†] prepared hydroxymethylenecamphor. Although this is the most convenient method for its preparation,[‡] this important derivative has also been obtained by the action of sodium methoxide on the α-mono- and di-halogenated camphors,[§] by the action of ethyl formate on α-bromocamphor in the presence of magnesium,[||] and by the decarboxylation of camphorglyoxylic acid.[¶] *Hydroxymethylenecamphor* crystallises in leaflets, m.p. 81°, and it is somewhat unstable, undergoing slow decomposition if it is kept. It is readily volatile in steam and is soluble in alkalis. In alcoholic solution it gives with ferric chloride a red violet coloration, which passes through blue to dark green. Considerable attention has been paid to the question of the constitution of hydroxymethylenecamphor. As was pointed out by Claisen, three formulae, (LI), (LII) and (LIII), are theoretically


(LI)


(LII)


(LIII)

---

[*] Haller and Minguin, *ibid.* 1900, **130**, 1362; Rupe and Blechschmidt, *Ber.* 1918, **51**, 170.

[†] *Annalen,* 1894, **281**, 330.

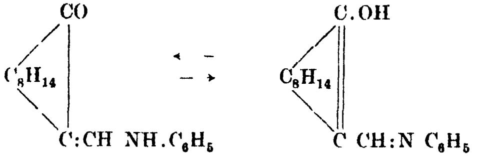
[‡] Compare Bredt and Sandkuhl, *ibid.* 1909, **366**, 62.

[§] Brühl, *Ber.* 1904, **37**, 2074.

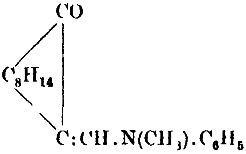
[||] Malmgren, *ibid.* 1903, **36**, 2635.

[¶] Langenbeck and Triem, *ibid.* 1936, **69**, 248.

possible. From an extended refractometric investigation, Bruhl* concluded that there was no evidence for the existence of two carbonyl groups in the molecule, and that the substance existed only in the stable enolic form (LII). A similar conclusion was reached by Federlin† from a series of colorimetric measurements in the presence of ferric chloride. Pope and Read‡ have shown, however, that solutions of hydroxymethylenecamphor show pronounced mutarotation; thus in benzene an initial value of $[\alpha]_D$ + 169·5° falls after twenty days to + 80·8°. They suggested that this is associated with a condition of dynamic isomerism between the two enolic forms (LII) and (LIII). This view receives support from the fact that whereas *d-anilomethylenecamphor* (LIV), in which this isomerism is possible, shows mutarotation, *d-methylanilomethylenecamphor* (LV) does not.



(LIV)



(LV)

There would appear to be no doubt that Pope and Read are correct, and that in solution hydroxymethylenecamphor is a mixture of the two enolic isomerides represented by (LII) and (LIII), although only derivatives of the enolic form (LII) and the ketonic form (LI) have been prepared. This investigation afforded a further example of the great value of the method, first introduced by Armstrong, for the determination of dynamic isomerism in the case of optically active substances.

The hydrogenation of hydroxymethylenecamphor gives a mixture of stereoisomeric *camphorylcarbinols* (LVI), b.p. 139–140°/9 mm.; two *benzoates* have been described, melting at 95–97° and 42–43°.§

On reduction with sodium in alcoholic solution hydroxymethylenecamphor yields a mixture of two stereoisomeric *glycols*,‖

---

[*] *Z. Phys. Chem.* 1900, **34**, 31.

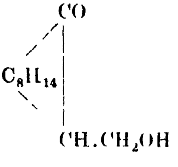
[†] *Annalen*, 1907, **356**, 251.

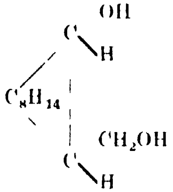
[‡] *J.C.S.* 1909, **95**, 175; compare Singh and Bhadhuri, *J. Ind. Chem. Soc.* 1930, **7**, 771; Bhagwat, Harmalker and Deshapande, *ibid.* 1940, **17**, 545.

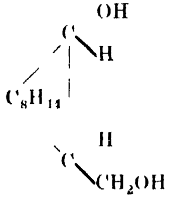
[§] Rupe and Lenzlinger, *Helv. Chim. Acta*, 1935, **18**, 255.

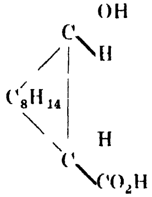
[‖] "Höchster Farbw." *G.P.* 123909.

which have been studied by Bredt.[*] The *cis*-glycol (LVII) melts at 101° and gives, on oxidation with potassium permanganate, camphoric acid, whilst the *trans*-glycol (LVIII), m.p. 117–118°, gives *trans*-borneolcarboxylic acid (LIX) (p. 451).

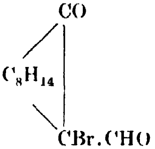

(LVI)

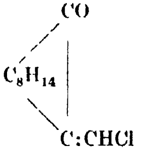

(LVII)

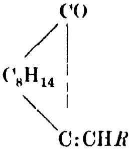

(LVIII)


(LIX)

On oxidation with potassium permanganate, hydroxymethylenecamphor yields camphoric acid, whilst by the action of chromic acid in acetic acid solution camphorquinone is obtained;[†] on ozonisation, both products are formed.[‡] Hydroxymethylenecamphor reacts readily with bromine, the nature of the product varying with the experimental conditions which are employed. In carbon disulphide solution or in faintly acid aqueous alcoholic solution *α-bromo-α'-formylcamphor* (LX), m.p. 44°, is obtained.[§] This substance is extremely unstable. By the addition of bromine to an aqueous solution of hydroxymethylenecamphor, α-bromocamphor is formed.[||]


(LX)


(LXI)

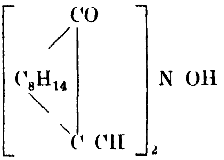

(LXII)

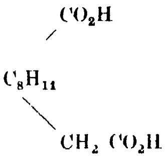
By the action of phosphorus trichloride or oxychloride chloromethylenecamphor (LXI), b.p. 113°/12·5 mm., $[\alpha]_D$ +180·28° (in benzene), is obtained. This chloride can, however, be prepared more conveniently by the action of thionyl chloride.[¶] It reacts readily with alkyl magnesium halides to yield alkylidene camphors (LXII), and this is probably the simplest method for the preparation of these derivatives of camphor.

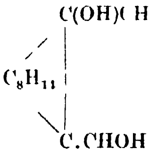
---

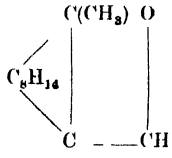
[*] *Annalen*, 1906, **348**, 199; 1909, **366**, 1.
[†] Bishop, Claisen and Sinclair, *ibid.* 1894, **281**, 330.
[‡] Palmén, *Finsk. Kem. Medd.* 1933, **42**, 85.
[§] Aschan and Bruhl, *Ber.* 1894, **27**, 2402.
[||] Bishop, Claisen and Sinclair, *Annalen*, 1894, **281**, 330.
[¶] Rupe and Iselin, *ibid.* 1916, **49**, 25.

Reference was made on p. 454 to the conversion of hydroxymethylenecamphor into α-cyanocamphor, and although the oxime of α-formylcamphor is an unstable oil, Johnson and Shelberg* have shown that when hydroxymethylenecamphor is treated with hydroxylamine hydrochloride in acetic acid solution it gives the *hydroxylimino*-compound (LXIII), which, on boiling with alkali, yields *homocamphoric acid* (LXIV). The *semicarbazone* is crystalline and melts at 217–218°.† With hydrogen cyanide, hydroxymethylenecamphor also reacts in the ketonic form to yield the corresponding cyanohydrin. Forster and Judd‡ have shown hydroxymethylenecamphor to react with methyl magnesium iodide to yield a substance which may be the *oxide* (LXVI), b.p. 234 /765 mm., the *glycol* (LXV) being evidently the primary product of the reaction.

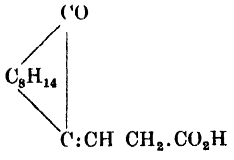

(LXIII)

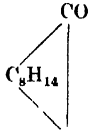

(LXIV)


(LXV)


(LXVI)

Hydroxymethylenecamphor condenses with malonic acid in the presence of pyridine to give an unsaturated acid, m.p. 104–106°, which is probably *camphorylidenepropionic acid* (LXVII). Similarly, cyanoacetic acid gives the corresponding *nitrile* (LXVIII), m.p. 72°.§


(LXVII)


(LXVIII)

---

* *J. Amer. Chem. Soc.* 1945, **67**, 1745, 1754.

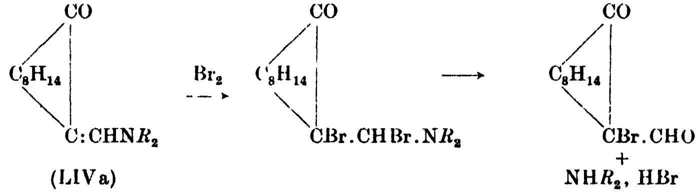
† Wallach and Steindorff, *Annalen*, 1903, **329**, 129.

‡ *J.C.S.* 1905, **87**, 372.

§ Borsche and Niemann, *Ber.* 1936, **69**, 1996.

Rupe and his collaborators[*] have studied several hydroxymethylenecamphor derivatives in their investigations on optical superposition.

In discussing the constitution of hydroxymethylenecamphor reference was made to the condensation products which it forms with aniline and methylaniline. This reaction is quite general, the condensation products having the formula (LIVa). Pope and Read[†] suggested the use of these derivatives for the resolution of externally compensated bases, since both *d*- and *l*-hydroxymethylenecamphors are available. Although the substituted methylenecamphors are stable to the ordinary hydrolytic reagents, they are frequently decomposed quantitatively by titration with an alcoholic solution of bromine in accordance with the scheme:[‡]



(LIVa)

This method is not, however, capable of general application, since, as in so many other cases, the formation of partial racemates occurs, and, further, the subsequent hydrolysis does not proceed smoothly.[§]

Acetylcamphor, which can theoretically exist in two isomeric modifications (XXXVI) and (XXXVIa) is probably most conveniently prepared by the action of ethyl acetate on α-bromocamphor in the presence of magnesium.[‖] It has also been obtained by the action of acetyl chloride and acetic anhydride on sodiocamphor and by the condensation of acetaldehyde and α-bromocamphor in the presence of magnesium.[¶] Reference was made on p. 455 to its preparation from cyanocamphor. Acetylcamphor is an oil, b.p. 118–118·5°/11·2 mm., $d^{18\cdot95^\circ}$ 1·0314, $n_D^{18\cdot95^\circ}$ 1·4938, and there can be no doubt that it consists mainly of the enolic modification (XXXVIa). Its solutions are acidic

---

[*] *Helv. Chim. Acta*, 1934, **17**, 271; 1936, **19**, 698; 1940, **23**, 53.

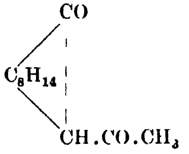
[†] *J.C.S.* 1913, **103**, 444.

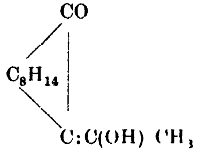
[‡] Pope and Read, *ibid.* 1912, **101**, 2337.

[§] Compare Gibson and Simonsen, *ibid.* 1915, **107**, 1150; Gibson, Kentish and Simonsen, *ibid.* 1928, p. 2133.

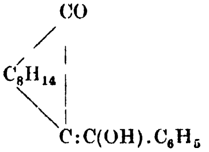
[‖] Brühl, *Ber.* 1904, **37**, 751.

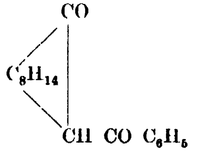
[¶] Malmgren, *ibid.* 1903, **36**, 2627.

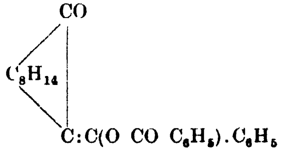

(XXXVI)

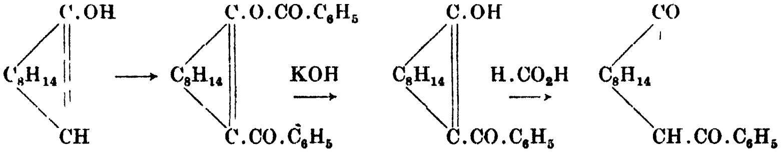

(XXXVIa)

and it dissolves readily in alkalis, whilst with ferric chloride in alcoholic solution it gives a purple red coloration changing through violet to indigo blue. It can be characterised by the preparation of the *oxime*, m.p. 164°. Although only one form of acetylcamphor is known, *benzoylcamphor* has been obtained in both the *enolic* (LXIXa) and *ketonic* (LXIX) forms. In 1901 Forster,* by the action of benzoyl chloride on sodiocamphor in toluene solution, prepared a dibenzoate, $C_{22}H_{24}O_3$, m.p. 144°, $[\alpha]_D$ +189·7°, which gave on hydrolysis with alkali a *monobenzoate*, $C_{17}H_{20}O_2$, m.p. 89°, $[\alpha]_D$ +281·1° (in chloroform), this initial value falling to a final value of +216°. Forster observed further that when this benzoate was digested for some hours with formic acid an isomeride was obtained, m.p. 87–88°, $[\alpha]_D$ +125° (in chloroform), the solution in this case also showing marked mutarotation, the value rising to +216°. It became obvious from these experiments that the two benzoyl derivatives were interconvertible and the change was found to be accelerated by piperidine and other catalysts. Forster originally considered the dibenzoate to be a derivative of the enolic form of camphor and he formulated the reactions occurring in accordance with the scheme:


(LXIXa)


(LXIX)


(LXX)

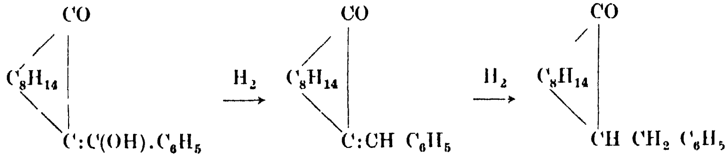


---

* *J.C.S.* 1901, **79**, 991.

Subsequent investigation[*] showed this to be incorrect, the dibenzoate being represented by (LXX), the two isomeric monobenzoates by (LXIX a) and (LXIX) respectively. The assignment of (LXIX a) to the enolic form is supported by the fact that on oxidation with chromic acid it yields camphorquinone, a substance extremely unlikely to be formed by the oxidation of a derivative of the enolic form of camphor.

The enol, which in alcoholic solution gives with ferric chloride an intense purple coloration, is readily soluble in alkali. It is reduced by sodium amalgam to *benzylidenecamphor* (LXXI) and *benzylcamphor* (LXXII).



(LXIX a) (LXXI) (LXXII)

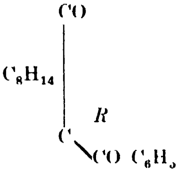
The ketonic form, which has been prepared also by the action of either benzaldehyde, methyl benzoate or benzoyl chloride on α-bromocamphor in the presence of magnesium,[†] is insoluble in alkali, and in alcoholic solution only slowly develops a colour with ferric chloride due to its conversion into the enolic modification.

In view of the theoretical interest of these two isomerides they have been exhaustively studied by Dimroth,[‡] Vixseboxse,[§] Lowry and Burgess[‖] and by Lowry, MacKonkey and Burgess.[¶] These elaborate physico-chemical investigations, for details of which the original memoirs should be consulted, have confirmed the structures assigned by Forster to the two benzoylcamphors. There can be no doubt that in all its reactions benzoylcamphor reacts in one or the other of these two isomeric forms, although there are five possible isomerides. In one particular only does Forster's work require alteration. The melting-point of the

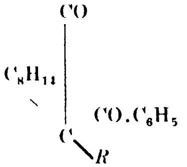
[*] Forster, *J.C.S.* 1903, **83**, 98.
[†] Malmgren, *Ber.* 1903, **36**, 2629.
[‡] *Annalen*, 1913, **399**, 110.
[§] *Rec. trav. chim.* 1921, **40**, 1.
[‖] *J.C.S.* 1923, **123**, 2122.
[¶] *Ibid.* 1928, p. 1333.

ketonic modification is 112°, the lower value previously recorded being due to the fact that isomerisation occurs if the melting-point is taken in the ordinary manner.

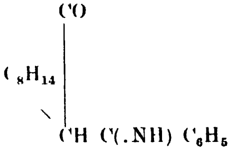
On chlorination, bromination and nitration of benzoylcamphor, substitution at the α-carbon atom occurs and the resulting derivatives have been obtained in both the stereoisomeric modifications (LXXIII) and (LXXIIIa).[*] When the enolic modification is heated with ammonium formate at 200–220° in a sealed tube *iminobenzoylcamphor* (LXXIV), m.p. 118–119°, $[\alpha]_D$ +235·2°, is obtained;[†] this substance can also be prepared by the action of phenyl magnesium bromide on α-cyanocamphor.[‡] The imine on hydrolysis yields enolic benzoylcamphor.



(LXXIII)

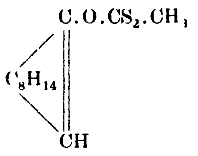


(LXXIIIa)

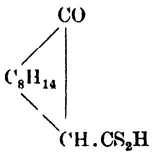


(LXXIV)

Tschugaev and Pigulewski[§] have shown that sodiocamphor when treated with carbon disulphide does not yield the xanthate (LXXV) but the sulphur analogue of camphor-3-carboxylic acid, *camphor-3-dithio-carboxylic acid* (LXXVI), the methyl ester of which boils at 179°/8 mm., $[\alpha]_D$ +424·58°.



(LXXV)



(LXXVI)

---

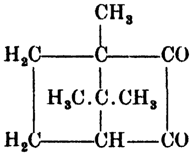
[*] Forster and Mickelthwait, *J.C.S.* 1902, **81**, 167; Forster and Jenkinson, *ibid.* 1903, **83**, 542.

[†] Forster, *ibid.* 1903, **83**, 108.

[‡] Forster and Judd, *ibid.* 1905, **87**, 372.

[§] *Compt. rend.* 1911, **153**, 388.

CAMPHORQUINONE



In 1893 Claisen and Manasse[*] made the important observation that when sodiocamphor was treated in ethereal solution with *iso*amyl nitrite a nitrosoderivative, iso*nitrosocamphor*, was obtained.[†] This substance was later prepared by Oddo[‡] by the action of nitrous acid on camphor-3-carboxylic acid and by the action of *iso*amyl nitrite on α-bromocamphor in the presence of sodium ethoxide.[§] *iso*Nitrosocamphor (I) prepared by any of these methods is not homogeneous (see below) and is the monoxime of *camphorquinone* (II), to which it can be readily hydrolysed by warming with formaldehyde and hydrochloric acid.[‖]

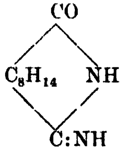
Evans, Ridgion and Simonsen[¶] have described the most satisfactory method for the preparation of camphorquinone, which is obtained in excellent yield by the oxidation of camphor (IV) with selenium dioxide in acetic anhydride solution.[**] It is also obtained by the action of the same reagent on epicamphor (V)[††] or on borneol (VI).[‡‡]

The diketone crystallises in golden yellow needles, m.p. 198°, $[\alpha]_D$ $-105{\cdot}4°$ (in chloroform), when prepared from *d*-camphor;

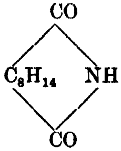
---

[*] *Annalen*, 1893, **274**, 530; compare Rupe and Splittgerber, *Ber.* 1907, **40**, 4313.

[†] A base $C_{10}H_{16}ON_2$, m.p. 278°, is always formed during the preparation of *iso*nitrosocamphor. This has been shown by Egli (*Helv. Chim. Acta*, 1929, **12**, 270) to be represented by formula (A), since it yields on treatment with sodium nitrite camphorimide (B).



(A)



(B)

[‡] *Gazzetta*, 1893, **23**, 187.

[§] Clarke, Lapworth and Wechsler, *J.C.S.* 1908, **93**, 40.

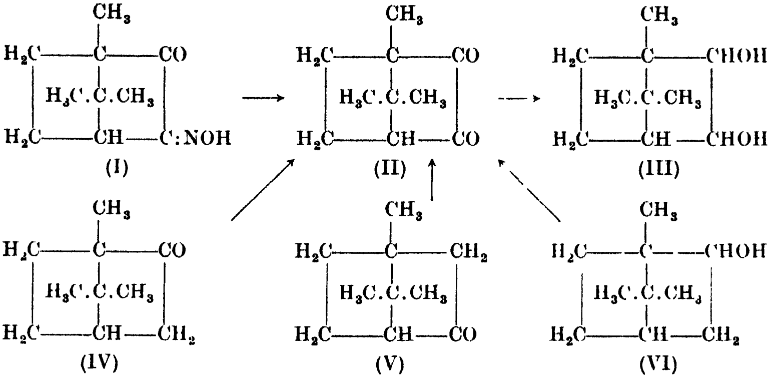
[‖] Lapworth, *ibid.* 1907, **91**, 1134.

[¶] *Ibid.* 1934, p. 137.

[**] Compare Vène, *Compt. rend.* 1943, **216**, 772.

[††] Asahina, Ishidate and Momose, *Ber.* 1934, **67**, 1432.

[‡‡] Allard, *Bull. Inst. Pin*, 1934, p. 127.



it is very volatile in steam. Its constitution has been established by its oxidation with hydrogen peroxide to camphoric acid,* fission of the ring occurring also when the diketone is digested with an alcoholic solution of potassium hydroxide.† On reduction with aluminium amalgam, or with zinc dust and acetic acid, a mixture of hydroxycamphor and hydroxyepicamphor is obtained (p. 427). This mixture of alcohols on further reduction with sodium in alcoholic solution yields *camphorglycol* (III), m.p. 230–231°, $[\alpha]_D$ +12·3°.‡ The glycol can also be obtained by hydrogenation of camphorquinone over a nickel catalyst, and when prepared by either method is a mixture of stereoisomers, the properties of which have been investigated by Häfliger§ and by Rupe.‖ Separation of *cis*- and *trans*-forms was accomplished by reaction with acetone, since the *cis*-glycols gave *iso*propylidene derivatives, the *trans*-forms being unaffected. The two possible *trans*-glycols have thus been obtained, and although they both melt at 230–231° they possess different rotatory powers, $[\alpha]_D^{20°}$ +9·8° and +17·8°, in alcohol. So far, only one of the *cis*-isomers has been obtained in crystalline form; it has m.p. 253–255°, $[\alpha]_D^{20°}$ −17·7°, in alcohol. On oxidation with lead tetra-acetate, the glycols give *camphoric dialdehyde*, m.p. 97°, *disemicarbazone*, m.p. 230°, *di*-p-*nitrophenylhydrazone*, m.p. 239°.

---

[*] Forster and Holmes, *J.C.S.* 1908, **93**, 252; compare Hollemann, *Rec. trav. chim.* 1904, **23**, 171.

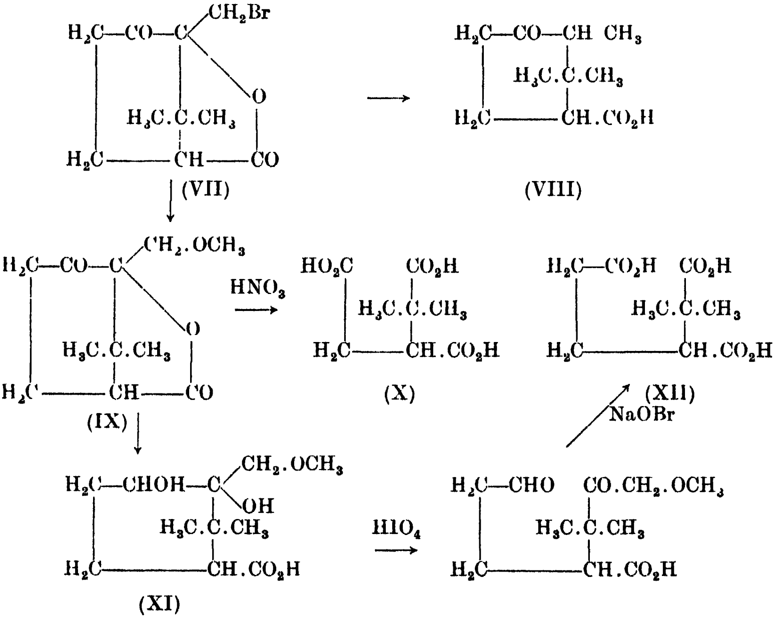
[†] Claisen and Manasse, *Annalen*, 1893, **274**, 83; Aschan, *Ber.* 1894, **27**, 1449.

[‡] Manasse, *ibid.* 1897, **30**, 659; 1902, **35**, 3811.

[§] *Helv. Chim. Acta*, 1940, **22**, 139.

[‖] Rupe and Muller, *ibid.* 1941, **24**, 265 E; Rupe and Thommen, *ibid.* 1947, **30**, 933.

By the action of bromine on camphorquinone, Manasse and Samuel[*] prepared two *bromides*, $C_{10}H_{12}O_3Br_2$, m.p. 137–138°, and $C_{10}H_{11}O_3Br_3$, m.p. 197–198°, $[\alpha]_D$ $-34°$. By hydrogenation of the latter in the presence of platinum black, the dibromide is formed, which on reduction with zinc dust in acetic acid solution yields a *monobromide*, $C_{10}H_{13}O_3Br$, m.p. 144°, $[\alpha]_D$ $+75{\cdot}25°$, and, on further action, d-2:2:3-*trimethylcyclohexan*-4-*one*-1-*carboxylic acid* (VIII). This monobromide gives on digestion with sodium methoxide a methoxy derivative (IX), $C_{11}H_{16}O_4$, m.p. 80–81°, which yields, on oxidation, *αα-dimethylpropane-αβδ-tricarboxylic acid* (X). When the methoxy-compound is hydrogenated, and the lactone ring then opened, it gives a *glycol* (XI), which on oxidation with periodic acid, followed by sodium hypobromite, yields *β-methylpentane-βγε-tricarboxylic acid* (XII). The monobromide is therefore represented by (VII), the reactions being shown in the following scheme:[†]

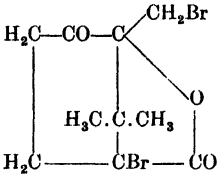


---

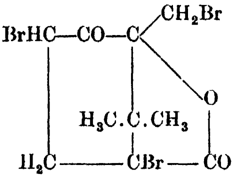
[*] *Ber.* 1897, **30**, 3160.

[†] Evans, Simonsen and Bhagvat, *J.C.S.* 1934, p. 444.

The structures of the di- and tri-bromides are not known with certainty, but the most probable formulae would appear to be (XIII) and (XIV) respectively.



(XIII)



(XIV)

When camphorquinone is dissolved in concentrated sulphuric acid it is converted into d-2:2:3-*trimethyl*cyclo*hexan*-4-*one*-1-*carboxylic acid* (VIII).[*] The formation of this acid which, as mentioned above, is obtained also from the monobromide (VII) involves a Wagner rearrangement.[†] According to Chakravarti,[‡] who has confirmed the structure and described a partial synthesis of the acid, the synthesis claimed by Guha and Gupta[§] is erroneous. When the diketone is treated with fuming sulphuric acid the monocyclic diketone, iso*camphorquinone* (XV), is obtained,[||] the constitution having been determined by Bredt, Rochussen and Mohnheim.[¶] Camphorquinone reacts with hydrogen cyanide to yield *α-hydroxy-α-cyanocamphor*, m.p. 197–198°,[**] whilst with methyl magnesium iodide the *glycol* (XVI), m.p. 132°, $[\alpha]_D$ +0·95°, is obtained.[††] With phenylmagnesium bromide, two structurally isomeric products are obtained, *phenylhydroxy*epi*camphor*, m.p. 193°, and *phenylhydroxycamphor*, m.p. 114–115°.[‡‡] The condensation of camphorquinone with ethyl sodiocyanoacetate, nitromethane and phenylacetonitrile has been investigated by Forster and Withers.[§§] By the action of ethyl orthoformate on camphorquinone the *acetal*, b.p. 126–128°/12 mm.,

---

[*] Bhagvat and Simonsen, *J.C.S.* 1927, p. 77; compare Gibson and Simonsen, *ibid.* 1925, **127**, 1295; Bredt-Savelsberg, Zaunbrecher and Knieke, *Ber.* 1927, **60**, 1801; Chakravarti, *J. Ind. C.S.* 1943, **20**, 301.

[†] Compare Ingold, *Ann. Reports*, 1927, **24**, 122.

[‡] *J.C.S.* 1947, p. 1565.

[§] *J. Indian Inst. Sci.* 1939, **22**, 255.

[||] Manasse and Samuel, *Ber.* 1898, **31**, 3259; 1902, **35**, 3836.

[¶] *Annalen*, 1901, **314**, 389.

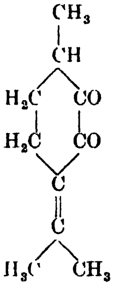
[**] Lapworth and Chapman, *J.C.S.* 1901, **79**, 381; Lapworth, *ibid.* 1903, **83**, 996; 1904, **85**, 1210.

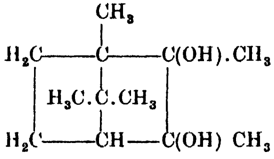
[††] Forster, *ibid.* 1905, **87**, 241; compare Briusova, *J. Gen. Chem. Russ.* 1939, **9**, 905.

[‡‡] Gripenberg, *Suomen Kem.* 1946, **19 B**, 46.

[§§] *J.C.S.* 1912, **101**, 1327.

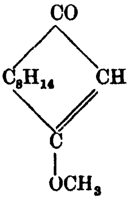
$d^{10\cdot8°}$ 1·0095, $n_D^{12\cdot5°}$ 1·4649, $[\alpha]_D$ +61·04° (in alcohol), is obtained. It yields on reduction, followed by hydrolysis with mineral acid, 2-hydroxyepicamphor.*

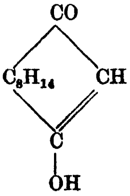

(XV)

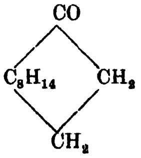

(XVI)

When heated with ammonia, camphorquinone gives *α-iminocamphor*; with methylamine, however, it yields a mixture of *3-methylaminocamphor* and *2-methylaminoepicamphor*, the reagent in this instance functioning also as a reducing agent.† On further reduction, the latter compounds give a stereoisomeric mixture of methylaminohydroxycamphanes.‡

Camphorquinone reacts vigorously with diazomethane to give *4-methoxy*-3 : *4-dehydrohomocamphor* (XVII), m.p. 54–55° (*oxime*, m.p. 195–196°), together with a liquid stereoisomer (*oxime*, m.p. 185–185·5°). On hydrolysis, the parent *homocamphorquinone*, m.p. 218–222°, is obtained, which exhibits strongly acid properties and is therefore assigned the enolic modification by Rupe and Frey § and formulated as *4-hydroxy*-3 : *4-dehydrohomocamphor* (XVIII). On hydrogenation, this is converted into *homocamphor* (XIX), m.p. 192–193° (*oxime*, m.p. 165°).


(XVII)


(XVIII)


(XIX)

---

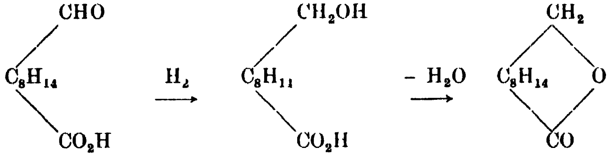
* Bredt-Savelsberg and Bund, *J. pr. Chem.* 1931 [ii], **131**, 29.

† Rupe and Vignano, *Helv. Chim. Acta*, 1937, **20**, 1078.

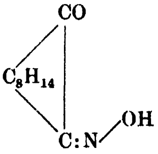
‡ Compare Mazza and Migliardi, *Ber.* 1939, **72**, 689.

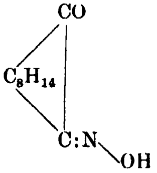
§ *Helv. Chim. Acta*, 1944, **27**, 627.

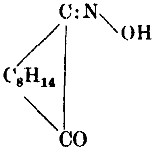
Bredt* has shown that on fusion with potassium hydroxide camphorquinone yields the tert.-*semialdehyde* of *camphoric acid* (XX), m.p. 76–78°, the formation of which from 2-hydroxyepicamphor has already been described on p. 428. The constitution of the aldehyde was proved by its electrolytic reduction to the *alcohol* (XXI) which passes readily into *β-campholide* (XXII).

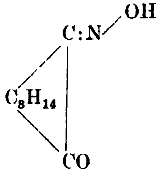

(XX) (XXI) (XXII)

Results of very great interest have been obtained from a study of the oximes, semicarbazones, hydrazones and phenylhydrazones of camphorquinone, and for our knowledge of these we are indebted mainly to the elaborate investigations of Forster and his collaborators. If the formula of camphorquinone be inspected, it is obvious that it can give rise to four monoximes, two *syn*- and two *anti*-, represented by formulae (XXIII), (XXIV), (XXV) and (XXVI). The two former are *iso*nitrosocamphors and the two latter *iso*nitrosoepicamphors.


(*syn*) (XXIII)


(*anti*) (XXIV)


(*syn*) (XXV)


(*anti*) (XXVI)

It was mentioned above that when *iso*nitrosocamphor is prepared by the Claisen method the product is not homogeneous. By fractional crystallisation, or more conveniently by treatment of the crude *iso*nitrosoderivative with ferric chloride in ethereal solution, Forster† obtained the stable modification of *iso*nitrosocamphor, m.p. 152°, $[\alpha]_D$ +197° (in chloroform), pure and free from the lower melting unstable isomeride. The latter, m.p. 114°,

---

* *J. pr. Chem.* 1917 [ii], **95**, 63; compare Baer, *J. Amer. C.S.* 1942, **64**, 1416.
† *J.C.S.* 1903, **83**, 538.

$[\alpha]_D$ + 172·9° (in chloroform), first obtained by a method which will be referred to later, can be separated from the crude Claisen mixture, of which it forms approximately one-half, by fractional decomposition of the sodium salt.[*] A supposed third modification of *iso*nitrosocamphor has been shown to be a mixture of these two. It is very unstable and passes on heating to 130–140° or on exposure to light into the stable form.

The configurations of these two oximes of camphorquinone were investigated by Forster,[†] who interpreted his results on the supposition, accepted at that time, that elimination reactions (such as dehydration) occurred more readily between *cis*- than between *trans*-groups. It has since been realised[‡] that this is not the case, and in the account that follows, which includes also some additional details described by Meisenheimer and Theilacker,[§] the conclusions to be drawn from Forster's experiments have been modified accordingly.

By the action of methyl magnesium iodide on the oxime an alcohol should result which, depending upon whether it was derived from the *syn*- (XXIII) or *anti*- (XXIV) form, would be represented by formulae (XXVII) and (XXVIII), or (XXIX) and (XXX), respectively.[‖] When the mixture of *iso*nitrosocamphors resulting from the Claisen reaction is treated with the Grignard reagent two alcohols are obtained: α-, m.p. 178°, and γ-, m.p. 195°.[¶] The latter alcohol is the sole product of the action of the Grignard reagent on the stable *iso*nitrosocamphor, m.p. 152°. When an alkaline solution of the γ-alcohol is warmed it immediately becomes turbid owing to the formation of the *keto-nitrile* (XXXI), m.p. 38·5°, which when hydrolysed by acid gives the *keto-acid* (XXXII), but under alkaline conditions yields *iminohomocamphor* (XXXIII), m.p. 248°; acid hydrolysis of the imino-compound gives *homocamphorquinone* (XXXIV), m.p. 223° (compare p. 470). The α-alcohol, however, is quite unaffected by this treatment. It follows, therefore, on the basis of a *trans*-elimination of water, that the α-alcohol must be represented by formulae (XXVII) or (XXVIII), and the γ-alcohol by either (XXIX) or (XXX). Since the γ-alcohol can be prepared from

---

[*] Forster and Rao, *J.C.S.* 1926, p. 2670.

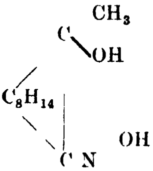
[†] *Ibid.* 1905, **87**, 232.

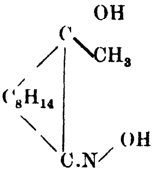
[‡] *Inter al.*, Taylor, *J.C.S.* 1931, p. 2021.

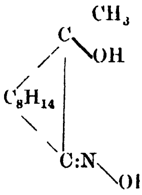
[§] *Annalen*, 1932, **493**, 33.

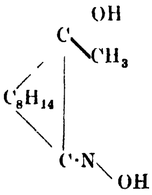
[‖] The group C:N.OH is in the plane of the paper, whilst the group $C(CH_3)OH$ is in a plane at right angles to the paper.

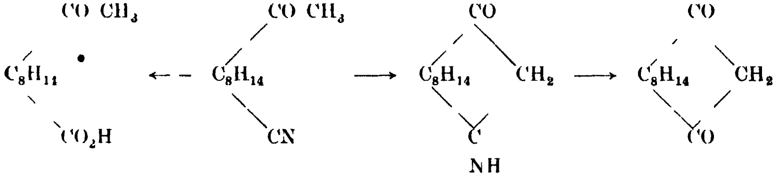
[¶] A "β"-form is now known to be a mixture of the α- and γ-alcohols.


(XXVII)


(XXVIII)

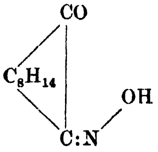

(XXIX)

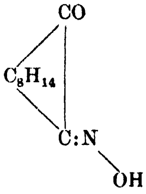

(XXX)

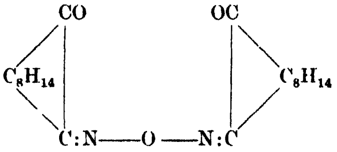

(XXXII) (XXXI) (XXXIII) (XXXIV)

the stable *iso*nitrosocamphor, m.p. 152°, it follows also that this must be anti-*camphorquinoneoxime* (XXIV), whilst the unstable modification, m.p. 114°, must be the syn-*camphorquinoneoxime* (XXIII).

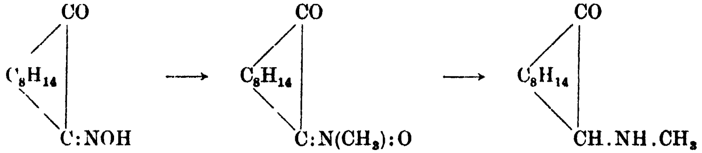
By the action of benzenesulphonyl chloride in pyridine solution, the *anti*oxime gives a *di-anhydride*, m.p. 154°, whilst the *syn*-oxime gives an isomer, m.p. 195°. These anhydrides are possibly stereoisomeric forms, of structure (XXXV).


(XXIII)

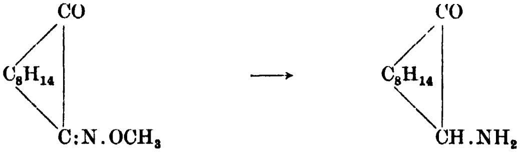

(XXIV)


(XXXV)

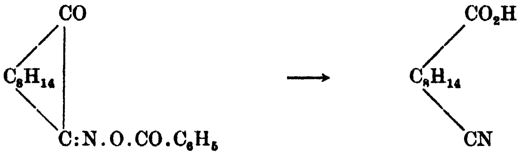
When the *anti*-oxime is treated with diazomethane, or its sodium derivative is treated with sodium methoxide in alcoholic solution, a yellow *methyl ether*, b.p. 188–192°/90 mm., is obtained, which is probably the *N*-methyl ether (XXXVI), since on reduction it yields *methylaminocamphor* (XXXVII). The *syn*-oxime gives the same ether when acted upon by diazomethane.[*]


(XXXVI) (XXXVII)

A second, colourless, methyl ether, m.p. 107°, probably the *O*-methyl ether (XXXVIII), was prepared from both the *syn*- and *anti*-oximes by the action of methyl iodide in the presence of silver oxide.[†] It is formed, together with the yellow ether, by the action of methyl iodide and sodium methoxide on both oximes. It differs from this in yielding on reduction with zinc dust *α-aminocamphor* (XXXIX).


(XXXVIII) (XXXIX)

Two benzoyl derivatives of *iso*nitrosocamphor have been prepared. The colourless *benzoyl* derivative, $C_{17}H_{19}O_3N$, m.p. 136°, is obtained when the *anti*-modification is treated with benzoyl chloride, either in pyridine or sodium hydroxide solution.[‡] It is reduced by zinc dust to aminocamphor, whilst by the action of methyl magnesium iodide dimethylaminocamphor is obtained. It is hydrolysed by alkali to *α-camphornitrilic acid* (XL) and is probably the *O*-benzoyl derivative (XLI).


(XLI) (XL)

---

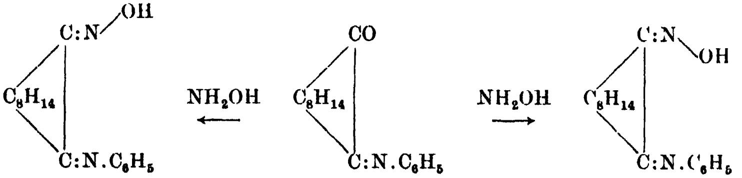
[*] Forster and Holmes, *J.C.S.* 1908, **93**, 244.

[†] Forster, *ibid.* 1904, **85**, 894; compare Ponzio and Charrier, *Gazzetta*, 1907, **37**, I, 510.

[‡] Forster, *J.C.S.* 1903, **83**, 527; 1904, **85**, 905; 1905, **87**, 234.

The yellow isomeric *benzoyl* derivative, m.p. 105–106°, which always accompanies the colourless isomer, can be obtained pure most readily by treatment of the *syn*-oxime with benzoyl chloride in cold pyridine solution. It yields the *syn*-oxime on hydrolysis with alcoholic ammonia. An analogous yellow m-*nitrobenzoyl* derivative, m.p. 136–137°, has been prepared, which is of interest, since by its hydrolysis Forster* was first able to isolate the pure *syn*-oxime.

The two *iso*nitrosoepicamphors (XXV) and (XXVI) were prepared simultaneously by Bredt and Perkin (see p. 519) from epicamphor and by Forster and Spinner.† The latter found that when *phenyliminocamphor* (XLII) was treated with hydroxylamine in alkaline solution two *phenyliminocamphoroximes* were obtained, the α-modification (XLIII) melting at 174°, $[\alpha]_D$ +304·4°, and the β- (XLIV) at 112°, $[\alpha]_D$ +335·4°. When the latter was ground up with cold dilute hydrochloric acid and the solution immediately filtered, it deposited β-iso*nitrosoepicamphor*, m.p. 137°, $[\alpha]_D$ −179·4° (in chloroform), rising to −191·4°. This substance, which was readily volatile in steam, gave a yellow *benzoyl* derivative, m.p. 80° and a yellow O-*methyl ether*, m.p. 77°. Like the low melting *iso*nitrosocamphor it was found to be unstable, and if its aqueous solution was boiled it passed into the stable α-modification, m.p. 170°, $[\alpha]_D$ −200·1° (in chloroform), falling to −191·0°.‡ From this a colourless *benzoyl* derivative was prepared, m.p. 122·5°, and both a colourless O-*methyl ether* and a yellow N-*methyl ether*. It will be observed that the α-isomeride behaves in an exactly similar manner to the stable modification of *iso*nitrosocamphor. In accordance with this, as might be anticipated, α-*iso*nitrosoepicamphor has the



(XLIII) (XLII) (XLIV)

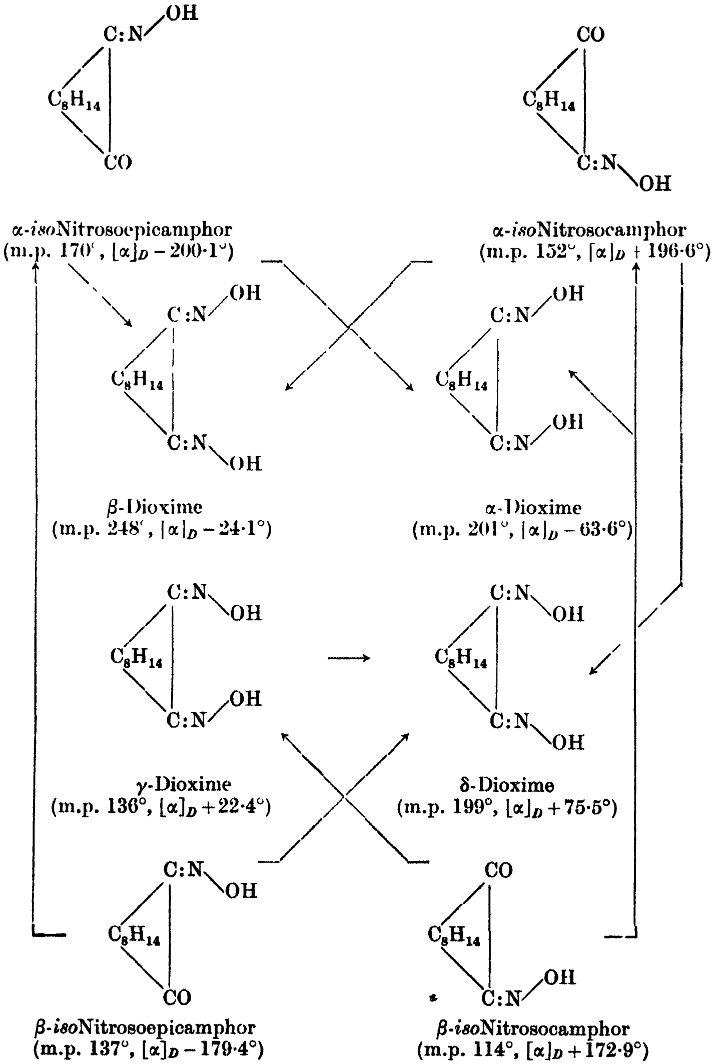
---

* *J.C.S.* 1904, **85**, 904.

† *Ibid.* 1912, **101**, 1340.

‡ The mutarotation of the two *iso*nitrosoepicamphors is due to the formation of an equilibrium mixture in solution.

anti-configuration (XXVI) and the β-modification the *syn*- (XXV) (p. 471). Their configurations were proved by methods identical with those employed in the case of the two *iso*nitrosocamphors.*



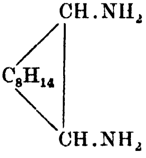
---

* Forster, *J.C.S.* 1913, **103**, 664.

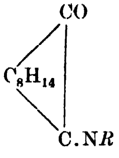
Corresponding to these four monoximes there are four dioximes of camphorquinone. These have all been prepared and their reactions studied very thoroughly by Forster and his collaborators. As the outcome of these elegant investigations, which it is unnecessary to discuss in detail, their configurations and their relationship to the monoximes have been determined. These are shown in the scheme on p. 476. By the reduction of camphorquinone dioxime with aluminium amalgam, Rupe and Bohny[*] have obtained 2.3-*diaminocamphane* (XLV), m.p. 148–149°; a stereoisomeric form of this diamine, b.p. 246°, is obtained when the reduction is carried out with sodium and alcohol.

Proceeding on similar lines, Forster and his collaborators have also studied the hydrazones, semicarbazones, hydrazo-oximes and oxime-semicarbazones of camphorquinone. Whilst the preparation of all the possible isomerides has not in all cases been realised, results of considerable interest have been obtained.[†]

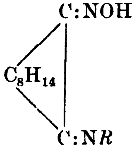
The facility with which camphorquinone condenses with aromatic amines to yield aryl derivatives of iminocamphor, having the general formula (XLVI), led Forster and Thornley[‡] to prepare a number of these in the hope that their oximes



(XLV)



(XLVI)



(XLVII)

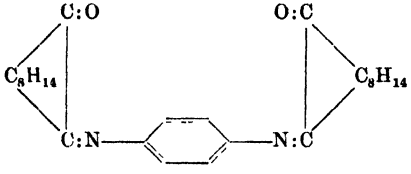
(XLVII) might on hydrolysis yield the then unknown *iso*nitroso-epicamphors. As will be obvious from the investigations discussed above, success was ultimately attained. Prior to this Forster and Thornley observed that the *bis*-iminocamphor derivatives possessed a remarkably high rotatory power. Thus in pyridine p-*phenylenebisiminocamphor* (XLVIII) has $[\alpha]_D$ + 1509°, giving a molecular rotatory power of 6096°. This is evidently connected with the high degree of conjugation present in the molecule.[*] The preparation of this type of derivative was continued by Singh and his collaborators,[†] who obtained substances having even higher rotatory powers.

---

[*] *Helv. Chim. Acta*, 1936, **19**, 1305.

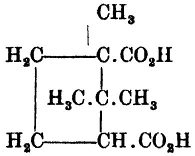
[†] *Inter al.*, Forster and Zimmerli, *J.C.S.* 1910, **97**, 2156; Forster and Kunz, *ibid.* 1914, **105**, 1718.

[‡] *Ibid.* 1909, **95**, 942.



(XLVIII)

CAMPHORIC ACID

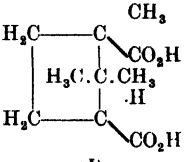


In the course of the discussion of the evidence bearing on the constitution of camphor (pp. 376–382) it was shown that this was based primarily on that of camphoric acid, which can be obtained readily by the oxidation of camphor itself and many of its derivatives. Whilst the formula for camphoric acid advanced in 1893 by Bredt accounted in a very simple manner for the majority of the reactions of the acid, yet a number of these were difficult to interpret. An attempt will now be made to survey the field without discussing in detail all the numerous investigations which have been carried out.

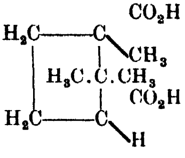
In 1893 there were recorded in the literature no fewer than thirteen camphoric acids; the Bredt formula permitted, however, the existence of only six. These are *d*- and *l*-*cis*-camphoric acids represented by formulae (I) and (Ia) and the externally compensated modification; the *d*- and *l*-*trans*-camphoric acids, generally designated *iso*camphoric acids (II) and (IIa) and the externally compensated form.

---

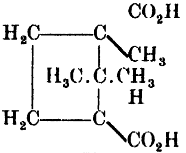
[*] Compare Forster and Spinner, *J.C.S.* 1919, **115**, 891.
[†] *Inter al.*, *J.C.S.* 1920, **117**, 1599; 1921, **119**, 1972.



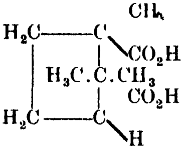
(I)



(Ia)



(II)



(IIa)

The investigations of Aschan[*] showed that actually only six camphoric acids existed, and that the others which had been described were mixtures. The melting-points and the optical rotatory powers of the acids are given in the following table:

	M.p.	$[\alpha]_D$
d- and *l*-Camphoric acid	187°	±47·8°
dl-Camphoric acid	202–203°	± 0°
d- and *l*-*iso*Camphoric acid	171–172°	±47·1°
dl-*iso*Camphoric acid	191°	± 0°

d-Camphoric acid, which has been used for most of the experiments to be discussed in the sequel, and which will be referred to simply as camphoric acid, is prepared as a rule by the oxidation of *d*-camphor with nitric acid. Its formation by the degradation of other derivatives of camphor has been referred to frequently in the preceding pages. Its optical enantiomorph, *l*-camphoric acid, was first obtained by Chautard[†] by the oxidation of *l*-camphor, and later by Jungfleisch[‡] and by Aschan[§] by the oxidation of *l*-borneol. *dl*-Camphoric acid was first prepared by Chautard by the admixture of equal quantities of *d*- and *l*-camphoric acids, it being obtained later by Armstrong and Tilden[||] by the oxidation of *dl*-camphor with nitric acid. In 1899 Debierne[¶] showed that it could be resolved into *d*- and *l*-camphoric acids by the crystallisation of its cinchonidine salt.

---

[*] *Ber.* 1894, **27**, 2001; *Acta Sci. Fennicae*, 1895 [v], **21**, 47; *Annalen*, 1901, **316**, 209.

[†] *Annalen*, 1857, **101**, 97; 1863, **127**, 121; *Compt. rend.* 1863, **56**, 698.

[‡] *Compt. rend.* 1890, **110**, 791.

[§] *Acta Sci. Fennicae*, 1895 [v], **21**, 49.

[||] *Ber.* 1879, **12**, 1756.

[¶] *Compt. rend.* 1899, **128**, 1112; compare Komppa, *Ber.* 1908, **41**, 4470.

As early as 1872 Wreden[*] had observed that camphoric acid was isomerised when it was heated with either hydriodic acid or hydrochloric acid in a sealed tube at 150–160°; to the acid prepared in this manner, he gave the name *meso*camphoric acid. The same change was found by Jungfleisch[†] to occur with water at 200–220°, but the pure laevorotatory *iso*camphoric acid was first prepared by Friedel,[‡] who showed that Wreden and Jungfleisch's *meso*camphoric acid was a mixture of *d*-camphoric acid and *d*-*iso*camphoric acid.

Later Mahla and Tiemann[§] found that isomerisation occurred also when camphoric acid was fused with potassium hydroxide. The separation of camphoric and *iso*camphoric acids by fractional crystallisation is most laborious, but this can be carried out quite readily by Aschan's method. In this, advantage is taken of the facility with which camphoric acid is converted into its anhydride by the action of acetyl chloride, when *iso*camphoric acid is unaffected and may be separated from the anhydride by solution in cold dilute alkali. For the preparation of *iso*camphoric acid the most convenient method is that devised by Walker and Wood.[‖] Camphoric acid is treated with phosphorus pentachloride and the mixture of acid chlorides poured into water at 80°. when the filtered solution deposits crude *iso*camphoric acid, which can be purified by Aschan's method. *iso*Camphoric acid does not yield an anhydride, but on heating gives camphoric anhydride. An equilibrated mixture of camphoric and *iso*camphoric acids is obtained when either acid is heated in a sealed tube in acetic-hydrochloric acid solution at 180°.

Camphoric acid can be most readily identified by the preparation of the *anhydride* (III), m.p. 220–221°, which, as mentioned above, is formed when the acid is heated with acetyl chloride. This anhydride has played an important part in the development of the chemistry of camphor. When reduced with sodium amalgam,[¶] or more conveniently catalytically,[**] it yields *α-campholide* (IV), m.p. 210–212°, $[\alpha]_D$ $-20{\cdot}2°$, a substance prepared also by Baeyer and Villiger[††] by the oxidation of camphor with Caro's reagent. Camphoric acid can give rise to two campholides, represented by formulae (IV) and (V); there can, however, be no doubt that α-campholide must be that represented by (IV), since it can be converted into the nitrile of homocamphoric acid either by the action of potassium cyanide (Haller) or by the action of hydrogen bromide, when the resulting *bromo-acid* (VI) gives, with potassium cyanide, the same *nitrile* (VII).* The acid, *homocamphoric acid* (VIII), obtained from this nitrile on hydrolysis is identical with that prepared from *α-cyanocamphor* (IX).† On alkaline hydrolysis, α-campholide gives *hydroxycampholic acid* (X), m.p. 119°.‡

---

[*] *Annalen*, 1872, **163**, 328.

[†] *Ber.* 1873, **6**, 680.

[‡] *Bull. Soc. chim.* 1874 [ii], **22**, 403.

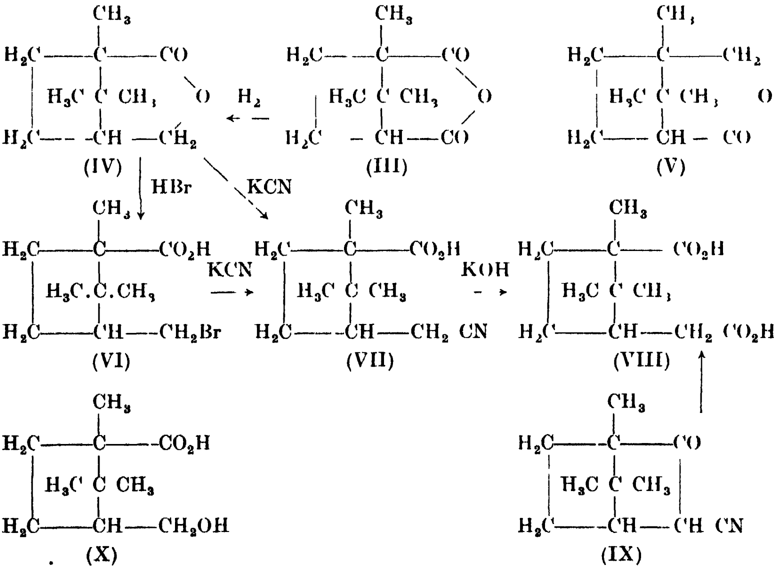
[§] *Ber.* 1895, **28**, 2153.

[‖] *J.C.S.* 1900, **77**, 386.

[¶] Haller, *Bull. Soc. chim.* 1896 [iii], **7**, 984; *Compt. rend.* 1900, **130**, 376.

[**] Rupe and Jäggi, *Helv. Chim. Acta*, 1920, **3**, 654.

[††] *Ber.* 1899, **32**, 3625.



Attention has been directed on p. 380 to the synthesis of camphor by the distillation of the calcium salt of homocamphoric acid and to its conversion into *camphononic acid* (XI). It will be convenient to summarise here the various methods by which this interesting acid has been prepared.

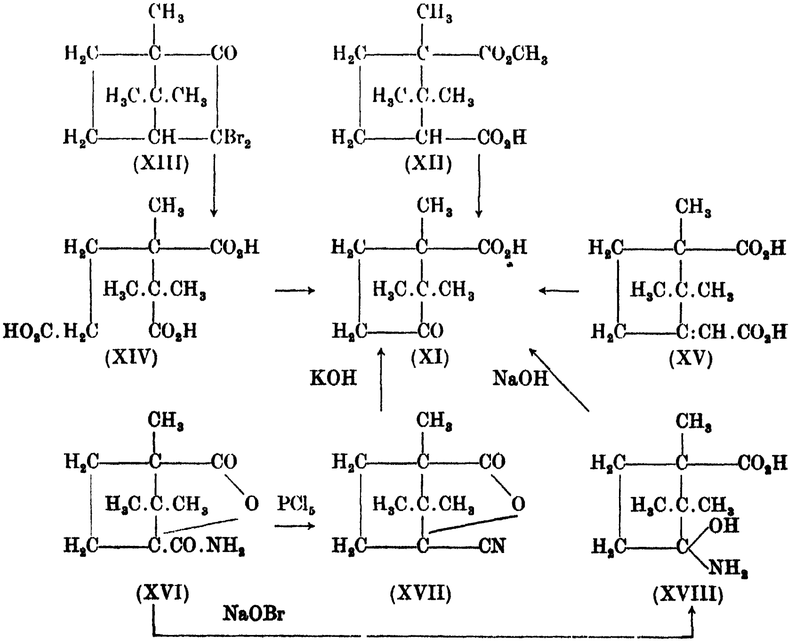
Camphononic acid, m.p. 228°, $[\alpha]_D$ +21·97°, was originally isolated by Walker and Henderson[*] in very small amount from amongst the products formed by the electrolysis of β-methyl hydrogen camphorate (XII), and it was next prepared by Lapworth and Chapman (compare p. 381) from αα′-dibromocamphor (XIII), whose degradation product, homocamphoronic acid (XIV), gave the ketonic acid when its lead salt was distilled. A more convenient method for the preparation of camphononic acid is by the oxidation of dehydrohomocamphoric acid (XV) (p. 381). Lapworth and Lenton[†] have further described its formation from camphanamide (XVI) by two distinct methods. In the first of these the amide was converted by the action of phosphorus pentachloride into the nitrile (XVII), which was readily hydrolysed by alkalis to the ketonic acid, whilst in the second the amide was treated with sodium hypobromite in the presence of excess of sodium hydroxide, when the ketonic acid was formed from the primary product, the unstable hydroxy-amino-acid (XVIII). These reactions are outlined in the scheme:

---

* Komppa, *Ber.* 1908, **41**, 4470.

† Lapworth, *J.C.S.* 1900, **77**, 1062.

‡ Salmon-Legagneur and Vène, *Bull. Soc. chim.* 1937 [v], **4**, 448.

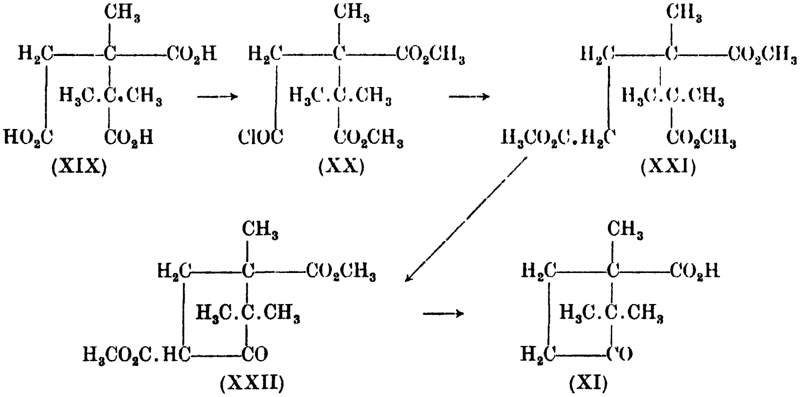


---

[*] *J.C.S.* 1896, 69, 755.

[†] *Ibid.* 1901, 79, 1286.

Ganguly* has described a synthesis of *camphononic* acid from synthetic *camphoronic acid* (XIX). When trimethyl camphoronate is partially hydrolysed, the primary ester group undergoes preferential saponification and it is possible, therefore, to prepare the mono-acid chloride (XX). Treatment of this with diazomethane and silver oxide, under the usual Arndt-Eistert conditions, gives *trimethyl homocamphoronate* (XXI), which undergoes cyclisation when treated in benzene solution with zinc and a trace of alcohol. The dimethyl 2:2:3-*trimethyl*cyclo*pentanone*-3:5-*dicarboxylate* (XXII) so obtained is hydrolysed and decarboxylated by heating with dilute sulphuric acid, and gives *dl*-camphononic acid (XI), m.p. 230–231°.


(XIX) (XX) (XXI) (XXII) (XI)

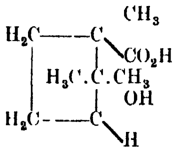
Camphononic acid cannot be reduced by sodium amalgam, resembling in this respect camphor-3-carboxylic acid, but Bredt† found that on electrolytic reduction a mixture of the *cis*- and *trans*-modifications of *camphonolonic acid* (XXIII) and (XXIII a), m.p. 197–198° and 249–250°, respectively, is obtained. The former acid passes readily into *camphonolactone* (XXIV), m.p. 160–161°, which was prepared originally by Noyes and Taveau‡ by the action of alkali on the *nitroso* derivative of the anhydride of 3-*aminocamphonanic acid* (XXV). When the *semicarbazone*, m.p. 225°, of camphononic acid is reduced with sodium ethoxide, it gives *camphonanic acid* (XXVI), m.p. 190–191°.[*]

---

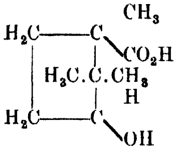
* *J. Ind. C.S.* 1943, **20**, 101.

† *J. pr. Chem.* 1911 [ii], **84**, 786; compare Noyes, Gorsline and Potter, *J. Amer C.S.* 1912, **34**, 62.

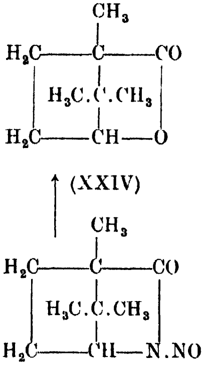
‡ *Amer. Chem. J.* 1906, **35**, 385.



(XXIIIa)

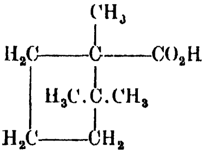


(XXIII)



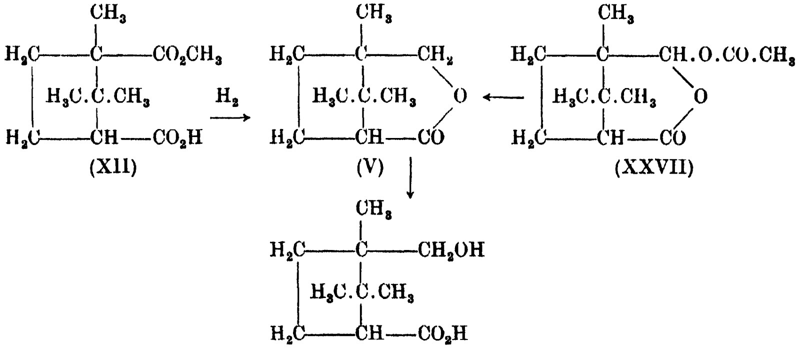
(XXIV)

(XXV)



(XXVI)

The isomeric *β-campholide* (V) was prepared by Haller and Blanc[†] by the reduction of *β-methyl hydrogen camphorate* (XII) with sodium in alcoholic solution. It was obtained also by Bredt[‡] by the reduction of the acetate of *hydroxy-β-campholide* (XXVII) prepared from the semi-aldehyde of camphoric acid (see p. 471). β-Campholide has m.p. 218–220°, $[\alpha]_D + 39{\cdot}2°$; it is extremely stable and it is not possible to convert it into a cyano-acid by the action of potassium cyanide, although on alkaline hydrolysis it gives the corresponding *hydroxy-acid* (XXVIII), m.p. 116–117°.[§]



(XII) (V) (XXVII)

(XXVIII)

---

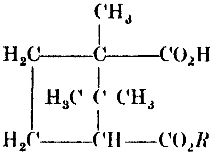
[*] Appel, *Z. Phys. Chem.* 1933, **218**, 202.

[†] *Compt. rend.* 1905, **141**, 697.

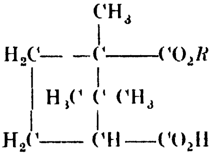
[‡] *J. pr. Chem.* 1917 [ii], **95**, 63.

[§] Salmon-Legagneur and Vène, *Bull. Soc. chim.* 1937 [v], **4**, 448.

Since camphoric acid is not symmetrical it can give rise to two isomeric hydrogen esters. These are designated α- or *ortho*-esters and β- or *allo*-esters, represented respectively by (XXIX) and (XXX), where *R* signifies an alkyl or aryl group.



(XXIX)
(α- or *ortho*-)



(XXX)
(β- or *allo*)

α- or ortho-*Methyl hydrogen camphorate* (XXIX), m.p. 77°, $[\alpha]_D$ +51·59, forms the main product when camphoric acid is esterified with alcohol containing either hydrogen chloride or sulphuric acid,[*] but, as Walker has shown, it can be prepared most conveniently by the addition of one molecular equivalent of sodium ethoxide to the equivalent quantity of camphoric anhydride in methyl alcoholic solution. β- or allo-*Methyl hydrogen camphorate* (XXX), m.p. 86–87°, can be prepared by the partial hydrolysis of the *dimethyl ester*.[†]

The constitution of these two esters would appear to be definitely established, the following being the main evidence in support of the formulae assigned to them: (i) in the case of similar unsymmetrical acids, treatment of the anhydride with sodium alkoxides causes esterification of the carboxyl group attached to the least substituted (α-) carbon atom;[‡] (ii) partial hydrolysis of the neutral esters always results in the preferential hydrolysis of the α-carboxyl group;[§] further, with 16 per cent. alkali the β-ester requires six hours for complete hydrolysis, whereas the α-ester is hydrolysed in thirty minutes;[‖] (iii) partial esterification results in the formation of the α-ester together with a little of the dimethyl ester: (iv) as measured by the electrolytic dissociation constants the β-hydrogen ester is the stronger acid;[¶] (v) the

---

[*] Bruhl and Braunschweig, *Ber.* 1892, **25**, 1807; Walker, *J.C.S.* 1892, **61**, 1088.

[†] Walker, *J.C.S.* 1893, **63**, 495; Walker and Henderson, *ibid.* 1895, **67**, 337; Haller and Blanc, *Compt. rend.* 1905, **141**, 697.

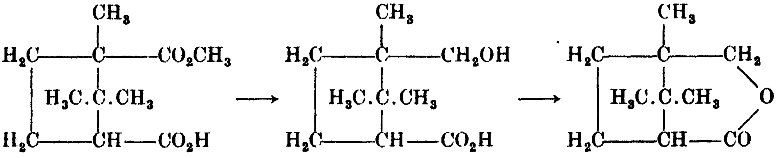
[‡] Blaise, *Bull. Soc. chim.* 1899 [iii], **21**, 716.

[§] Bone, Sudborough and Sprankling, *J.C.S.* 1904, **85**, 548.

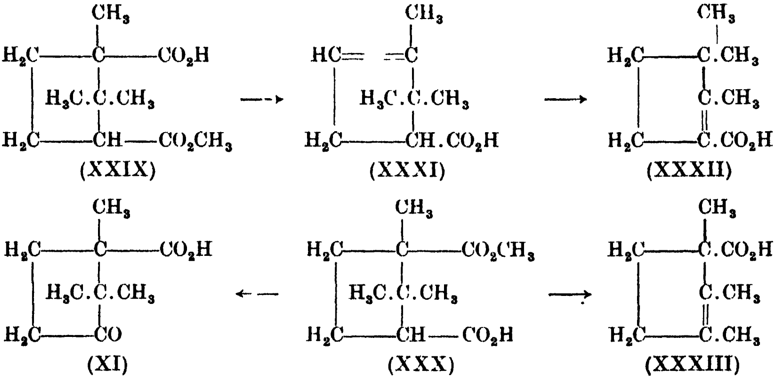
[‖] Bruhl and Braunschweig, *Ber.* 1892, **25**, 1806.

[¶] Walker, *J.C.S.* 1892, **61**, 1093.

β-ester (XXX) yields on reduction with sodium in alcoholic solution β-campholide (V), the alcohol (XXVIII) being an intermediate product of the reaction; (vi) on electrolysis of its sodium salt the α-ester (XXIX) yields a mixture of *α-campholytic acid* (XXXI) and iso*lauronolic acid* (XXXII); (vii) the sodium salt of the β-ester (XXX) on the other hand yields on electrolysis *laurolenic acid* (XXXIII) and *camphononic acid* (XI).*



(XXX) (XXVIII) (V)



(XXIX) (XXXI) (XXXII)

(XI) (XXX) (XXXIII)

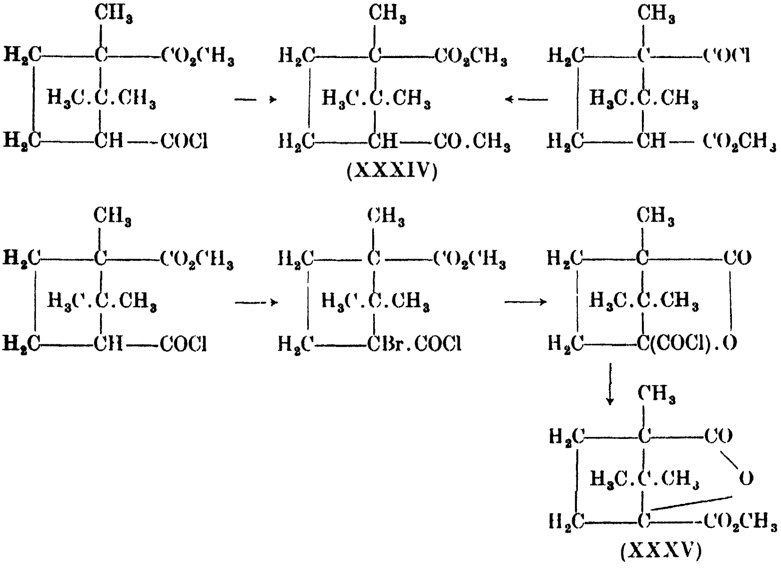
In spite of this apparently overwhelming body of evidence in favour of the structural isomerism of the α- and β-esters, it was suggested by Qudrat-i-Khuda† that they were actually stereoisomerides. This suggestion was based on the fact that, when either the α- or β-ester is treated with thionyl chloride, and the acid chloride, so prepared, is allowed to react with zinc methyl, the same ketonic ester (XXXIV) is obtained;‡ the corresponding acid melts at 73°.* The probability that the two esters were stereoisomerides was considered to be supported by the fact that they both yield on bromination of their acid chlorides, followed by the addition of methyl alcohol, methyl camphanate (XXXV), and that the α-ester is converted into the β-ester by the action of thionyl chloride and water.

---

* Walker and Henderson, *J.C.S.* 1896, **69**, 755; Lapworth and Chapman, *ibid.* 1899, **75**, 986; Bredt, *J. pr. Chem.* 1911 [ii], **83**, 395.

† *J.C.S.* 1930, p. 206.

‡ The preparation of the structurally isomeric ketonic ester is discussed on p. 501.



(XXXIV)

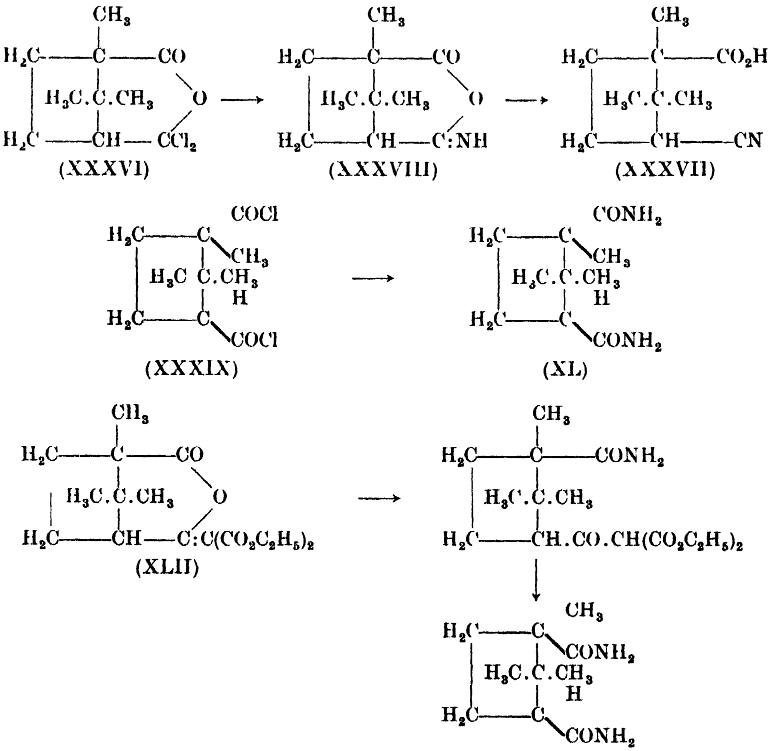
(XXXV)

These results can, however, be explained without making the assumption that the two esters are stereoisomerides. It is well known that dibasic acids, which readily give anhydrides, are not converted into their acid chlorides, but into their anhydrides, by the action of thionyl chloride. It seems therefore not improbable that, in this case also, an unstable chloroanhydride is formed which passes by molecular rearrangement into the more stable β-ester acid chloride. It would be of interest to repeat these experiments with the corresponding esters of *iso*camphoric acid, since it has been shown by Bredt† that when camphoric acid is treated with phosphorus pentachloride it yields a mixture of the acid chlorides of camphoric and *iso*camphoric acids,* the former of which has the unsymmetrical structure (XXXVI), since it yields on treatment with ammonia *α-camphornitrilic acid* (XXXVII), the *imine* (XXXVIII) being an intermediate product of the reaction (compare p. 490). The acid chloride of *iso*camphoric acid (XXXIX) has, however, the normal structure and yields with ammonia the trans-*diamide* (XL), m.p. 160 . The corresponding cis-*diamide* (XLI), m.p. 197–199°, was prepared by Winzer† by the action of ammonia on *ethyl camphorylmalonate* (XLII).‡ The reactions involved are shown in the scheme:

---

* Compare Winzer, *Annalen*, 1890, **257**, 311; Lapworth and Royle, *J.C.S.* 1920 **117**, 743.

† *Ber.* 1912, **45**, 1419.


(XXXVI) (XXXVIII) (XXXVII)

(XXXIX) (XL)

(XLII) (XLI)

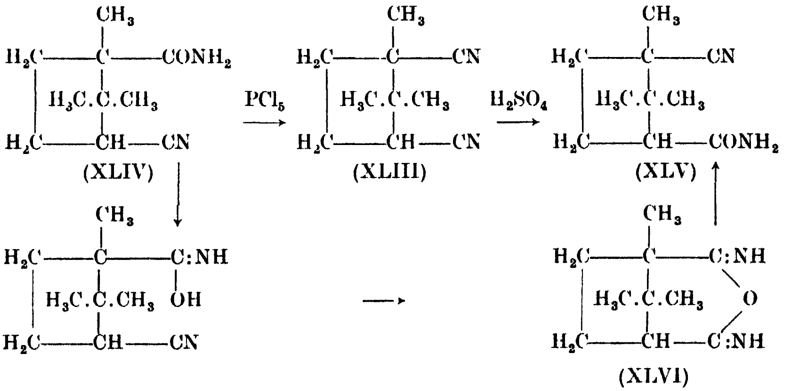
---

* Compare Walker and Wood, *J.C.S.* 1900, **77**, 386.

† *Annalen*, 1890, **257**, 307.

‡ Compare Buser and Rupe, *Helv. Chim. Acta*, 1943, **26**, 857. *Ethyl camphoryl acetoacetate* has been described by Rupe and Ziekendraht, *ibid.* 1946, **29**, 1529.

By dehydration of the diamides, *camphoric acid dinitrile* (XLIII), *cis*-, m.p. 160°; *trans*-, m.p. 144–145°, is obtained. Bredt and Souza* have studied the conversion of cis-α-*camphornitrilic β-amide* (XLIV) into the structural isomeride (XLV); this may be done either by conversion with phosphorus pentachloride into the *cis*-dinitrile (XLIII), followed by partial hydrolysis with sulphuric acid, or by direct isomerisation of the nitrilic amide with sulphuric acid. The latter change, which is obviously similar to the interconversion of the α- and β-esters discussed above, is considered by Lipp† to proceed through the intermediate formation of a di-iminoanhydride (XLVI), according to the scheme shown below:



A large number of both neutral and hydrogen esters of camphoric acid have been prepared, but these do not require separate mention.

Reference has already been made (p. 428) to the two structurally isomeric semialdehydes of camphoric acid.

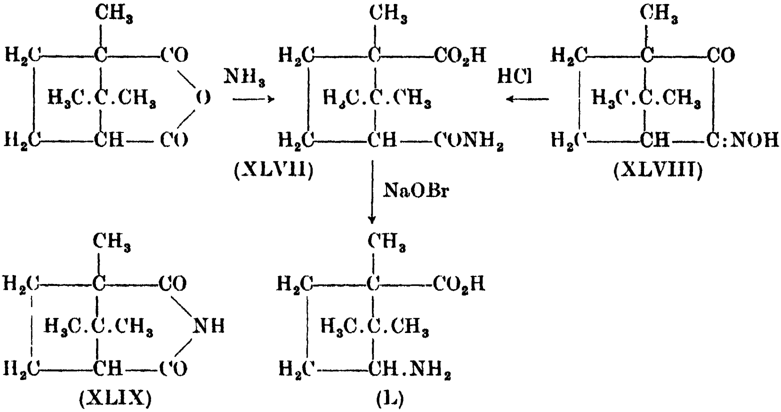
Corresponding to the two hydrogen esters of camphoric acid two monoamides have been prepared. The *α-amide* (*α-camphoramic acid*) (XLVII), m.p. 176–177°, is readily obtained by the action of ammonia on camphoric anhydride,‡ whilst it can be prepared also by warming *iso*nitrosocamphor (XLVIII) with concentrated hydrochloric acid.[*] The α-amide is reconverted into the anhydride when it is heated above its melting-point, but, if the ammonium salt is distilled, *camphorimide* (XLIX) is obtained. By the action of sodium hypobromite on the amide, Noyes[†] prepared *3-amino-camphonanic acid* (L).

---

* *J. pr. Chem.* 1932 [ii], **133**, 84.

† *Ibid.* p. 87.

‡ Laurent, *Annalen*, 1846, **60**, 327; Auwers and Schnell, *Ber.* 1893, **26**, 1522.

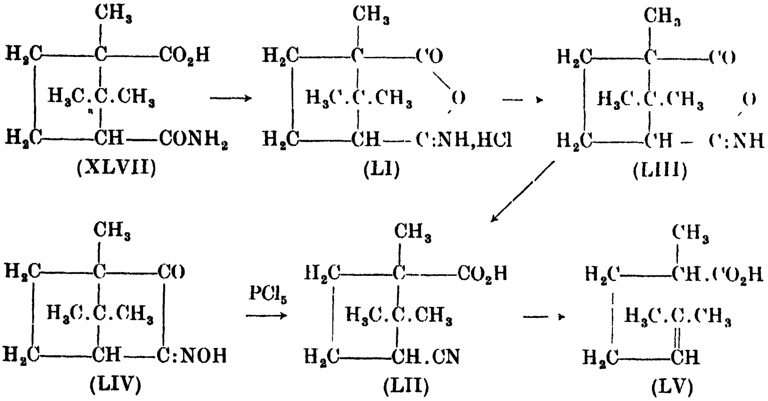


If α-camphoramic acid is heated with an excess of acetyl chloride, ring closure occurs with the formation of the hydrochloride of the imine (LI),[‡] which gives with ammonia *α-cyano-camphonanic acid* (*α-camphornitrilic acid*) (LII), m.p. 151–152°, by molecular rearrangement of the unstable *imine* (LIII). This cyano-acid can be prepared much more conveniently by treating *iso*nitrosocamphor (LIV) with phosphorus pentachloride and decomposing the chloride, so obtained, with water.[§] The calcium salt of the nitrile, like that of the isomeric nitrile (see p. 491), undergoes an interesting reaction when distilled, being converted into *α:ε-dimethyl-Δ^{δ}-heptenoic acid* (LV), camphorimide being an intermediate product of the reaction.[‖]

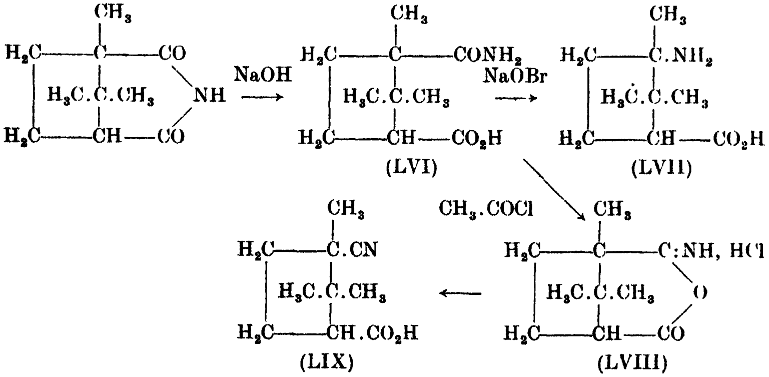
The isomeric *β-amide* (LVI) (*β-camphoramic acid*) of camphoric acid, m.p. 182–183°, is best prepared by warming camphorimide

---

[*] Claisen and Manasse, *Annalen*, 1893, **274**, 78.
[†] *Amer. Chem. J.* 1894, **16**, 506.
[‡] Hoogewerff and van Dorp, *Rec. trav. chim.* 1895, **14**, 262.
[§] Rupe and Splittgerber, *Ber.* 1907, **40**, 4313.
[‖] Bredt and Wornast, *Annalen*, 1903, **328**, 346.



with dilute sodium hydroxide solution.* When it is treated with sodium hypobromite it yields *aminodihydro-α-campholytic acid* (LVII). The *β*-amide behaves with acetyl chloride in exactly the same manner as its isomeride, yielding the *imine hydrochloride* (LVIII), which with ammonia gives *cyanodihydro-α-campholytic acid* (*β-camphornitrilic acid*) (LIX), m.p. 109–111°. On distillation of its calcium salt the heptene acid (LV) is obtained.



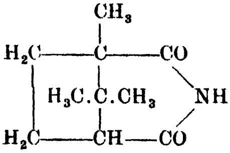
Wootton† has described a number of substituted amides which were obtained by the action of various bases on camphoric anhydride.

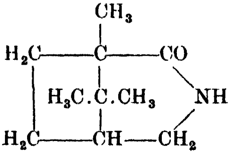
---

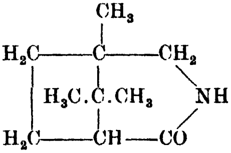
* Noyes, *Amer. Chem. J.* 1894, **16**, 310, 503; Rupe and Splittgerber, *Ber.* 1907, **40**, 4315.

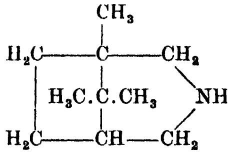
† *J.C.S.* 1910, **97**, 410.

Camphorimide (XLIX), m.p. 243–244°, was probably first obtained by Berzelius[*] by the distillation of the ammonium salt of the α-amide, but it is more conveniently prepared by the distillation of camphoric acid in a stream of ammonia.[†] In its general reactions it resembles phthalimide, and a number of substituted derivatives have been prepared by Evans.[‡] On electrolytic reduction Tafel and Eckstein[§] have shown that it yields *α-camphidone* (LX), m.p. 295°, *β-camphidone* (LXI), m.p. 225°, and *camphidine* (LXII), m.p. 209°. The constitution of α- and β-camphidones was established by Tafel and Bublitz[‖] by converting them, through their nitroso-derivatives, into α- and β-campholides. A simpler method for the preparation of α-camphidone consists in heating α-campholide with ammonia and zinc chloride in a sealed tube.[¶]


(XLIX)


(LX)


(LXI)


(LXII)

Being a saturated cyclic acid, camphoric acid is extremely stable to reducing agents. When it is heated at 200° in a sealed tube with hydriodic acid, it undergoes a molecular rearrangement with loss of carbon dioxide and formation of the hydrocarbon, *laurolene* (LXIII), the constitution of which is discussed on p. 512.[**] If red phosphorus be added to the hydriodic acid, then 1:3-*dimethyl*cyclo*hexane* (LXIV) is obtained.[††] These two hydrocarbons are formed also by the action of hydrochloric acid or phosphoric acid at high temperatures.

---

[*] Fehling's *Handwörterbuch*, **2**, 380.

[†] Bredt and Wornast, *Annalen*, 1913, **328**, 338.

[‡] *J.C.S.* 1910, **97**, 2237.

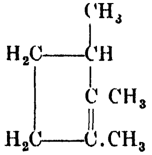
[§] *Ber.* 1901, **34**, 3277

[‖] *Ibid.* 1905, **38**, 3806.

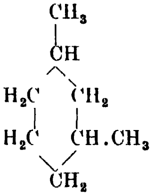
[¶] Rupe and Jäggi, *Helv. Chim. Acta*, 1920, **3**, 654.

[**] Walker and Henderson, *J.C.S.* 1896, **69**, 753.

[††] Balbiano and Angeloni, *Gazzetta*, 1904, **35**, I, 147.



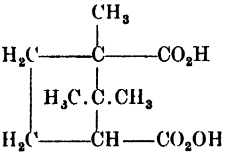
(LXIII)



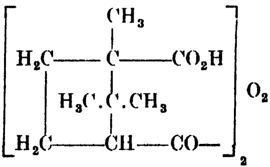
(LXIV)

Camphoric acid is remarkably stable to the action of oxidising agents. As was mentioned on p. 379, it gives on prolonged digestion with nitric acid camphoronic acid, whilst with potassium permanganate the most important product is Balbiano's acid (p. 380).

When *d*-camphoric anhydride in ethereal solution is added to aqueous sodium peroxide it gives d-*percamphoric acid* (LXV), m.p. 49–50°; if a deficiency of the peroxide, however, is added to the camphoric acid solution, *dicamphoryl peroxide* (LXVI), m.p. 142°, is obtained.*



(LXV)



(LXVI)

The products formed on fusion of camphoric acid with both sodium and potassium hydroxides have been studied in great detail by Crossley and Perkin.† They consist mainly of substituted acyclic acids. When the calcium salt of camphoric acid is distilled it yields *camphorone*, 1-*methyl*-3-iso*propylidene*cyclo*pentan*-2-*one* (LXVII), b.p. 200–202°, $d^{20°}$ 0·933, $n_D^{20°}$ 1·4824.‡

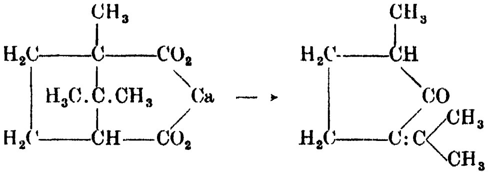
Other salts of camphoric acid behave differently on distillation. Thus the lead salt yields mainly camphoric anhydride, together with a little camphorone,[*] whilst from the copper salt iso*laurolene* (LXVIII) can be obtained.[†] Other methods for the preparation of this hydrocarbon are described later.

---

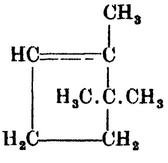
* Milas and McAlevy, *J. Amer. C.S.* 1933, 55, 349.

† *J.C.S.* 1898, 73, 3.

‡ *Inter al.*, Wallach and Collmann, *Annalen*, 1904, 331, 320.

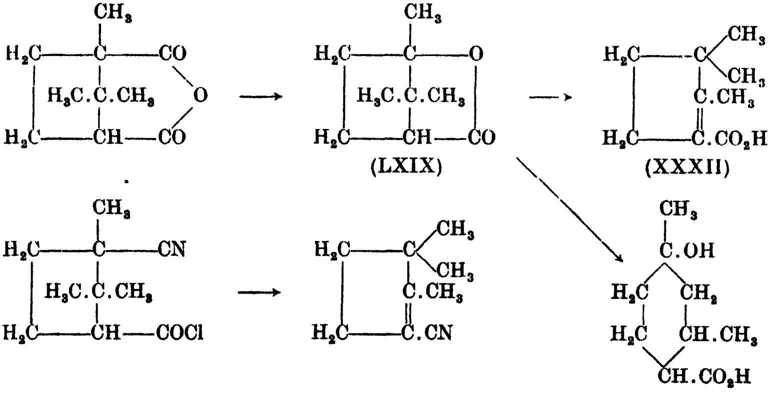


(LXVII)



(LXVIII)

Results of considerable interest have accrued from a study of the action of aluminium chloride on camphoric anhydride. Following a preliminary investigation by Burcker,[‡] Blanc[§] showed the main product of the reaction to be *iso*lauronolic acid. As the outcome of a more thorough investigation Lees and Perkin[‖] and Perkin and Yates[¶] found that, in addition to iso*lauronolic acid* (XXXII), four stereoisomeric 1 : 3-*dimethyl*-1-*hydroxy*cyclo*hexane*-4-*carboxylic acids* (LXX) were formed. It is probable that the mechanism of the reaction is the following. By elimination of carbon monoxide camphoric anhydride passes into *α-campho-*



(LXIX) (XXXII)

(LXXI) (LXXII) (LXX)

---

[*] Bouosein, *Arch. Pharm.* 1855, **133**, 277.

[†] Moitessier, *Jahresbericht*, 1866, p. 410.

[‡] *Compt. rend.* 1894, **119**, 426; *Bull. Soc. chim.* 1895 [iii], **13**, 901.

[§] *Compt. rend.* 1896, **123**, 746; **124**, 468; *Bull. Soc. chim.* 1896 [iii], **15**, 1191; 1900 [iii], **23**, 693.

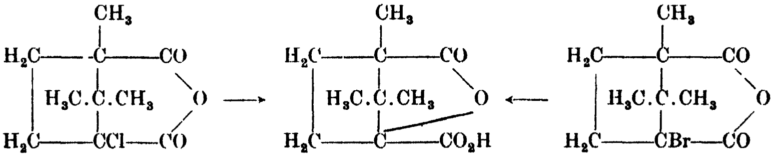
[‖] *J.C.S.* 1901, **79**, 332.

[¶] *Ibid.* 1373.

lytolactone (LXIX) which decomposes in two directions: (i) with loss of water and wandering of one of the *gem*-dimethyl groups to give *iso*lauronolic acid, and (ii) with a wandering of one of the *gem*-dimethyl groups into the ring, so converting a five into a six-membered ring.

A similar change occurs when the *chloride* (LXXI) of *α-camphornitrilic acid* is treated with aluminium chloride in chloroform solution, *isolauronolonitrile* (LXXII) being obtained.[*]

The hydrogen atom attached to the α- (or 3-) carbon atom in camphoric acid can be replaced readily by halogen with the formation of monohalide derivatives. *α-Chlorocamphoric anhydride* (LXXIV), m.p. 233–235°, was prepared by Marsh and Gardner[†] by pouring chlorocamphoric acid dichloride, obtained by the action of an excess of phosphorus pentachloride on camphoric acid, into water. It can be prepared also by the action of chlorine on the acid chloride.[‡] Like the bromo-anhydride (see below), on digestion with alkali or with water it is converted into the lactonic acid, *camphanic acid* (LXXV).


(LXXIV) (LXXV) (LXXVI)

α-Bromocamphoric anhydride (LXXVI) can be prepared by the bromination of either camphoric anhydride[§] or the acid bromide.[||] It is best hydrated to the corresponding acid by warming for a few minutes with concentrated nitric acid.[¶] When either the acid or its anhydride is boiled with water, dilute alkali, or in acetic acid solution with potassium acetate,[**] it is converted mainly into camphanic acid, a little laurolenic acid (p. 509) being formed simultaneously. The important experiments of Lapworth and

---

[*] Salmon-Legagneur, *Compt. rend.* 1935, **200**, 1222.

[†] *J.C.S.* 1896, **69**, 81.

[‡] Aschan, *Acta Sci. Fennicae*, 1895, **21**, no. 5, 214.

[§] Wreden, *Annalen*, 1872, **163**, 330; Fittig and Woringer, *ibid.* 1885, **227**, 1.

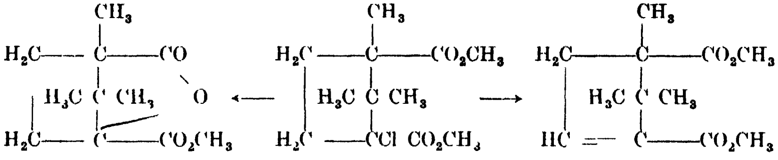
[||] Aschan, *Ber.* 1894, **27**, 2116, 3505.

[¶] Kipping, *J.C.S.* 1896, **69**, 63.

[**] Aschan, *Acta Sci. Fennicae*, 1895, **21**, no. 5, 221.

Lenton on the conversion of camphanic acid into camphononic acid were discussed on p. 482.

Although α-bromocamphoric anhydride yields on treatment with alkali only the lactonic acid and no unsaturated acid containing the camphoric acid nucleus, Bredt and his collaborators* showed that when *methyl α-chlorocamphorate* (LXXVII), m.p. 56°, is distilled at the ordinary pressure it yields a mixture of *methyl dehydrocamphorate* (LXXVIII), b.p. 137°/15 mm., and *methyl camphanate* (LXXIX). The former can, however, be prepared in better yield by the distillation of *phenyl α-chlorocamphorate*, m.p. 89°.



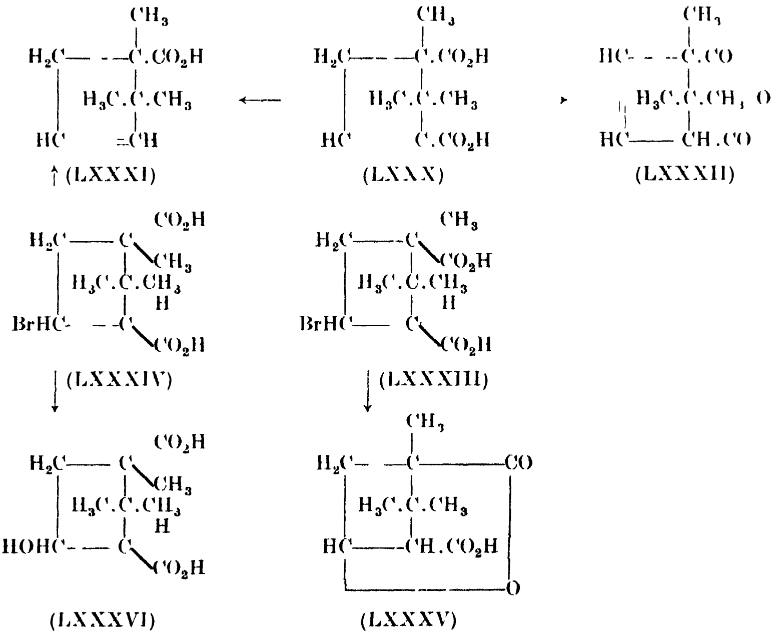
(LXXIX) (LXXVII) (LXXVIII)

On hydrolysis, methyl dehydrocamphorate yields *dehydrocamphoric acid* (LXXX), *d*-form, m.p. 202–203°, $[\alpha]_D$ +118·6°, which, on distillation at the ordinary pressure, yields a mixture of *camphonenic acid* (LXXXI) and iso*dehydrocamphoric anhydride* (LXXXII), m.p. 185·5–186°, iso*dehydrocamphoric acid* melting at 181–182°.

Dehydrocamphoric acid, which yields on oxidation with dilute potassium permanganate camphoronic acid, does not give an anhydride. When heated at 100° with hydrobromic acid, it yields a mixture of cis- and trans-4-*bromocamphoric acids* (LXXXIII) and (LXXXIV), melting at 158–160° and 232°, respectively. On reduction with zinc dust in acetic acid solution the *cis*-acid yields camphoric acid and the *trans*-acid *iso*camphoric acid. They differ also in their behaviour towards sodium carbonate solution, since the *cis*-bromo-acid gives 4-*hydroxycamphorolactone* (LXXXV), m.p. 228°, whilst the *trans*-acid gives trans-4-*hydroxycamphoric acid* (LXXXVI), m.p. 194°, and *camphonenic acid* (LXXXI). Owing to the possibility of Walden inversion during replacement of the bromine atom, the formation of the lactone (LXXXV) does not necessarily show that the bromine atom in (LXXXIII) is *cis*- with respect to the tertiary carboxyl group; a *trans*-configuration would, in fact, be more probable.

---

* *Annalen*, 1913, **395**, 26.



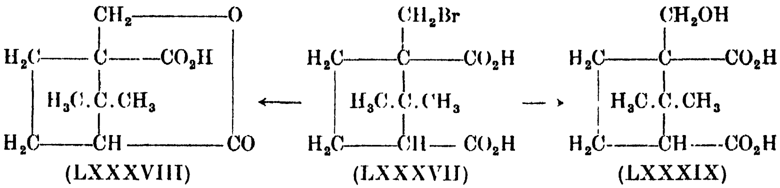
Of the remaining halogen acids derived from camphoric acid, mention need only be made of ω-(6-)*bromocamphoric acid* (LXXXVII), m.p. 208–210°, *anhydride*, m.p. 142°, prepared by Armstrong and Lowry* by the oxidation of ω-bromocamphor (p. 404), and *π-bromocamphoric acid* (XC), m.p. 216–217°, *anhydride*, m.p. 155–156°, obtained by Kipping† by the oxidation of απ-dibromocamphor (p. 408) with nitric acid.

When treated with silver oxide, *dl*-ω-bromocamphoric acid gives dl-*ω-camphanic acid* (LXXXVIII), m.p. 151–152°, whilst when heated with dilute alkali it gives the corresponding hydroxy-acid, dl-*ω-hydroxycamphoric acid* (LXXXIX), m.p. 158–159°.*

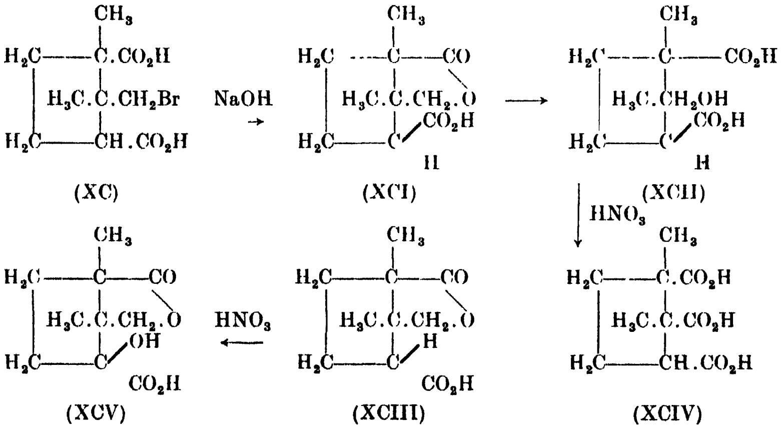
---

* *J.C.S.* 1902, **81**, 1467.

† *Ibid.* 1896, **69**, 913; Lapworth and Kipping, *ibid.* 1897, **71**, 12.


(LXXXVIII) (LXXXVII) (LXXXIX)

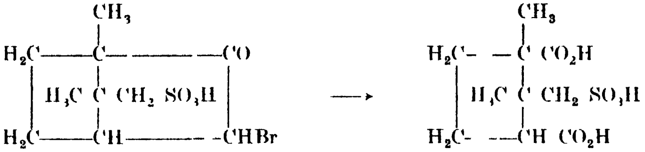
When π-bromocamphoric acid is warmed with dilute sodium hydroxide it yields the sodium salt of trans-*π-camphanic acid* (XCI), m.p. 164–165°, from which, by boiling with an excess of alkali and acidification, the corresponding hydroxy acid, trans-*π-hydroxycamphoric acid* (XCII), m.p. 131°, can be prepared. This acid, when distilled, loses water with the formation of a new lactone, cis-*π-camphanic acid*, m.p. 226°. The hydroxy acid corresponding to this lactonic acid is extremely unstable and cannot be obtained pure. These two lactones are, according to Kipping, the stereoisomerides represented by (XCI) and (XCIII), the *cis*-acid being a derivative of *iso*camphoric acid. They differ in a remarkable manner in their stability to oxidising agents, since, whereas the *trans*-acid is readily oxidised by nitric acid to trans-*camphotricarboxylic acid* (XCIV), m.p. 195–196°, the *cis*-acid yields cis-*hydroxy-π-camphanic acid* (XCV), m.p. 264–265°.


(XC) (XCI) (XCII) (XCV) (XCIII) (XCIV)

---

* Komppa, *J. pr. Chem.* 1943 [ii], 162, 19.

Camphoric acid cannot be directly sulphonated, but the *π-sulphonic acid* (XCVII) was prepared by Lapworth and Kipping* by the oxidation of *α-bromocamphor-π-sulphonic acid* (XCVI) with an ammoniacal solution of potassium permanganate. It melts at 188° with the formation of the *anhydride*, m.p. 220–222°. This anhydride can be converted readily into the corresponding *sulphonyl chloride*, m.p. 184–185°, or *bromide*, m.p. 169–170°, which, when heated above their melting-points, yield respectively *π-chloro-* and *π-bromo-camphoric anhydrides*.



(XCVI) (XCVII)

When camphoric acid (or camphoric anhydride) is warmed with concentrated sulphuric acid, an unsaturated sulphonic acid, *sulphocamphylic acid*, $C_9H_{14}O_5S$, is obtained.† This acid is formed also when *iso*lauronolic acid (XXXII) is treated with concentrated sulphuric acid. The reactions of this interesting sulphonic acid were studied in very great detail by Perkin,‡ who concluded that it was represented by formula (XCVIII) and that, in its preparation from camphoric acid, *iso*lauronolic acid was formed as an intermediate product. Lewis and Simonsen,§ however, have shown that it is 2:3:3-*trimethyl*-Δ^1-cyclo*pentene*-1-*carboxylic*-4-*sulphonic acid* (XCIX). On oxidation with nitric acid it gives dimethylmalonic and oxalic acids, together with *β-sulpho-αα-dimethylglutaric acid* (C) which on pyrolysis gives *αα-dimethylglutaconic acid* (CI).‖ When sulphocamphylic acid bromide is heated at 155° it gives an unsaturated bromo-acid (CII), the structure of which is proved by ozonisation to the bromoketo-acid (CIII) which on further oxidation with sodium hypobromite yields bromoform and αα-dimethylglutaconic acid (CI). The alternative structure (CIV) for the bromo-acid was rejected, since it had already been assigned to *iso*bromodihydro-β-camphylic acid (p. 501), with which the above bromo-acid was not identical.

---

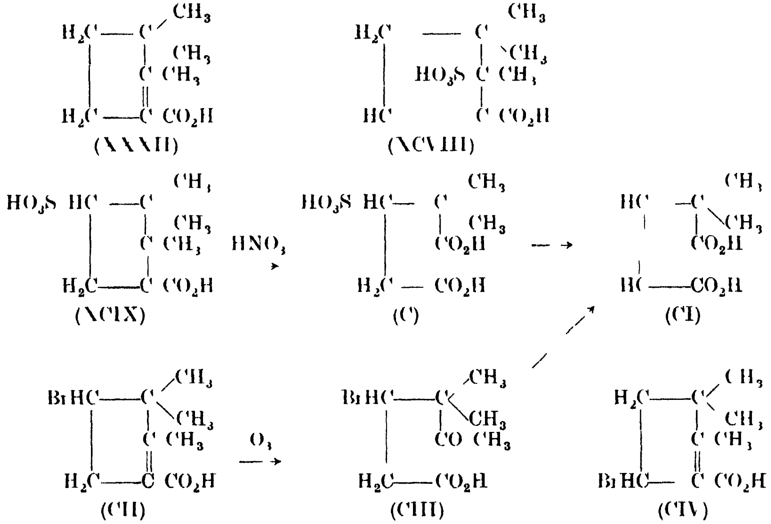
* *J.C.S.* 1897, **71**, 8.

† Walter, *Ann. Chim.* 1843 [iii], **9**, 179; Kachler, *Annalen*, 1873, **169**, 179; Damsky, *Ber.* 1887, **20**, 2959; Koenigs and Hoerlin, *ibid.* 1893, **26**, 812; 1894, **27**, 3466; Perkin, *J.C.S.* 1898, **73**, 798.

‡ *J.C.S.* 1898, **73**, 798; *ibid.* 1903, **83**, 835.

§ *Ibid.* 1937, p. 457.

‖ This was erroneously identified by Koenigs and Hoerlin (*Ber.* 1893, **26**, 812) as terebic acid.



(XXXII) (XCVIII)

(XCIX) (C) (CI)

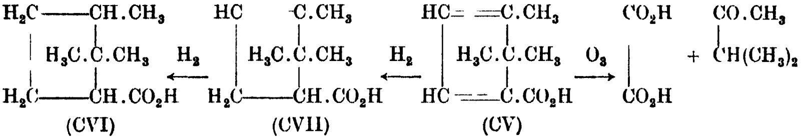
(CII) (CIII) (CIV)

The recognition of sulphocamphylic acid as a sulpho*iso*lauronolic acid suggests that the primary action of sulphuric acid on camphoric acid is to give α-campholytic acid, which isomerises in the presence of the mineral acid to *iso*lauronolic acid; the latter then undergoes sulphonation without further molecular rearrangement.

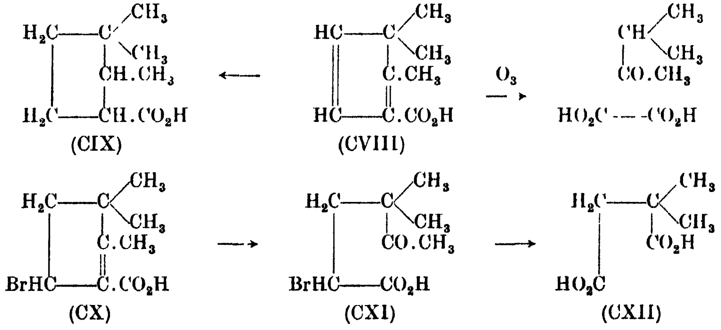
If sulphocamphylic acid is heated at 210–220° or distilled in steam at 170–190° it is converted into *iso*lauronolic acid.[*] By fusion with sodium hydroxide Perkin obtained two isomeric acids, *α-camphylic acid*, m.p. 148°, and *β-camphylic acid*, m.p. 105–106°.[†] The structures of these acids have been determined by Lewis and Simonsen,[‡] α-camphylic acid being represented by (CV). It contains a conjugated system of two ethylenic linkages, and gives a crystalline *adduct*, m.p. 106°, by condensation of its

[*] Koenigs and Hoerlin, *Ber.* 1893, **26**, 813.
[†] Compare Alder and Windemuth, *Annalen*, 1939, **543**, 28.
[‡] *J.C.S.* 1936, p. 734.

methyl ester with α-naphthaquinone. On hydrogenation it gives *dihydro-α-campholytic acid* (CVI), whilst oxidation with ozone gives methyl *iso*propyl ketone and oxalic acid. Perkin observed that on reduction with sodium amalgam it gave *α-campholytic acid* (CVII).


(CVI) (CVII) (CV)

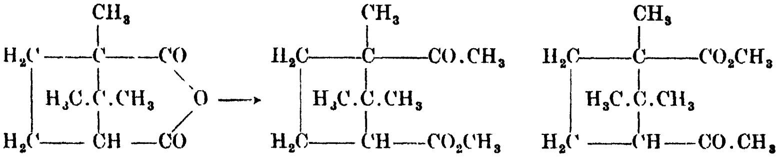
β-Camphylic acid (CVIII) also contains two conjugated ethylenic linkages, and its methyl ester gives an *adduct*, m.p. 135°, with α-naphthaquinone. On hydrogenation, *dihydro*iso*lauronolic acid* (CIX) is formed, whilst oxidation with ozone gives methyl *iso*propyl ketone and oxalic acid. With hydrogen bromide it yields iso*bromodihydro-β-camphylic acid* (*bromo*iso*lauronolic acid*) (CX), the structure of which is proved by ozonisation and subsequent oxidation of the *bromoketo-acid* (CXI) with sodium hypobromite to as-*dimethylsuccinic acid* (CXII).

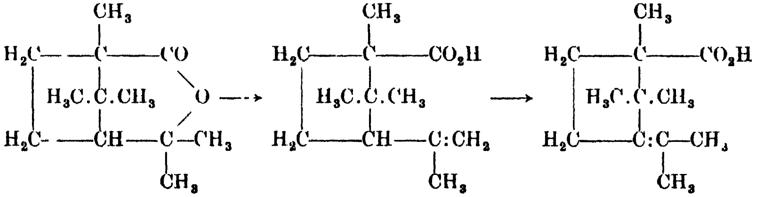

(CIX) (CVIII) (CX) (CXI) (CXII)

By the action of a limited amount of methyl magnesium iodide on camphoric anhydride, Komppa and Rohrmann* obtained a small yield of the *keto-ester* (CXIII) from which the corresponding acid was prepared; it crystallised with one mol. of water, and melted at 76–78° (*semicarbazone*, m.p. 223–224°). The ester is the structural isomer of the ketonic-ester (XXXIV) to which reference has been made on p. 486. With an excess of the Grignard reagent, *dimethylcampholide* (CXIV), m.p. 83·5–85°, is obtained, together with an unsaturated acid, m.p. 68°, to which is assigned formula (CXV), since on oxidation it gives the keto-acid corresponding to the ester (XXXIV); on repeated crystallisation, the melting-point of (CXV) rises to 87–88°, and this is considered to be due to a transformation of the *iso*propenyl form (CXV) into the *iso*propylidene structure (CXVI). Quantitative conversion of dimethylcampholide into the unsaturated acid is brought about by heating with 50 per cent. potassium hydroxide at 300°.

---

* *Annalen*, **1936**, **521**, **229**; compare Komppa, *Ber.* **1908**, **41**, **1039**.


(CXIII) (XXXIV)

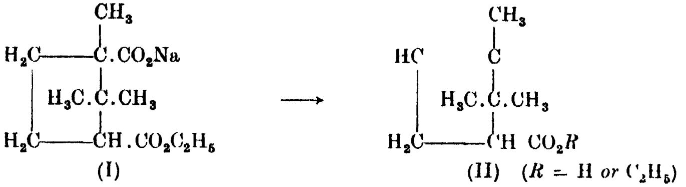

(CXIV) (CXV) (CXVI)

Some Degradation Products of Camphoric Acid. By the degradation of camphoric acid and its derivatives, a number of acids containing nine carbon atoms have been prepared, either the α- or β-carboxyl group having been eliminated. The determination of the structure of these acids has been attended with considerable difficulty, since many of them readily undergo the Wagner rearrangement. In the account which follows, those in which the tertiary (β-) carboxyl group has been eliminated will be considered first.

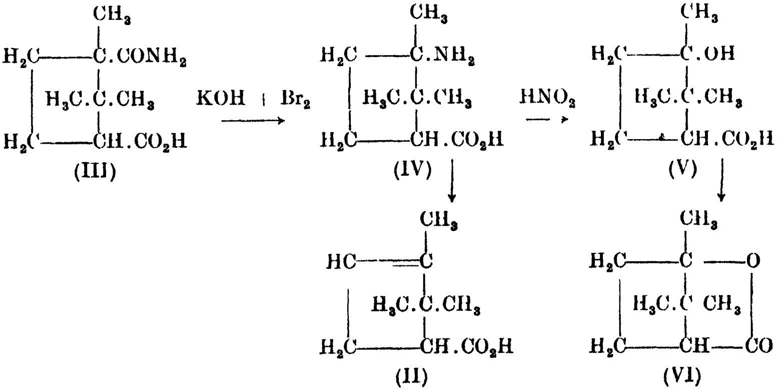
α-Campholytic acid, 1:1:2-*trimethyl*-Δ^2-cyclo*pentene*-5-*carboxylic acid* (II) was first prepared by Walker* by the electrolysis of the sodium salt of α-ethyl hydrogen camphorate (I), when hydrolysis of the ethyl ester, so obtained, gives an acid having a small laevorotation.

---

* *J.C.S.* 1893, **63**, 495.


(I) (II) (R = H or C_2H_5)

Shortly afterwards Noyes* prepared the acid by a completely different method. When β-camphoramic acid (III) is treated in alkaline solution with bromine it yields *aminodihydro-α-campholytic acid* (IV), which by the action of nitrous acid gives a mixture of *hydroxydihydro-α-campholytic acid* (V), *campholytolactone* (VI) and *α-campholytic acid* (II).

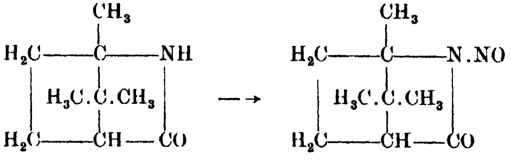

(III) (IV) (V) (II) (VI)

A more detailed study of this reaction was made by Noyes and Potter,† who found that when aminodihydro-α-campholytic acid is heated it yields an *anhydride* (VII) which gives with nitrous acid a *nitroso*-derivative (VIII), m.p. 188–189°, from which, by the action of alkali, *trans*-hydroxydihydro-α-campholytic acid, m.p. 133·7°, $[\alpha]_D$ +7·01°, together with some α-campholytic acid, campholytolactone and iso*laurolene* (IX), was prepared.

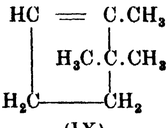
---

* *Amer. Chem. J.* 1894, **16**, 500; 1895, **17**, 424; Noyes and Phillips, *ibid.* 1900, **24**, 290.

† *J. Amer. C.S.* 1912, **34**, 1067.



(VII) (VIII)



(IX)

From the *trans*-hydroxy acid they prepared trans-*campholytolactone*, m.p. 115–117°, $[\alpha]_D$ +121·9°, which differed from cis-*campholytolactone*, m.p. 118–119°, $[\alpha]_D$ +8·5°. The latter lactone was first obtained by Tiemann and Kerschbaum[*] by the action of nitrous acid on aminodihydro-α-campholytic acid, and yields on solution in alkali and careful acidification cis-*hydroxydihydro-α-campholytic acid*, m.p. 118·5°, $[\alpha]_D$ +50·8°.[†]

α-Campholytic acid was synthesised by Perkin and Thorpe[‡] during the course of their synthesis of camphoric acid, which is described on p. 383. By the action of methyl magnesium iodide on ethyl 1:1-*dimethyl*cyclo*pentan-5-one-2-carboxylate* (X) they obtained a lactone, α-*campholactone* (XI), b.p. 155–157°, possibly a mixture of *cis*- and *trans*-campholytolactones. This lactone gave with hydrogen bromide 2-*bromo*-1:1:2-*trimethyl*cyclo*pentane-5-carboxylic acid* (hydrobromide of α-campholytic acid)[§] (XII), m.p. 108°, and from this by the action of sodium carbonate α-campholytic acid was obtained.

On oxidation with potassium permanganate α-campholytic acid yields *dihydroxydihydro-α-campholytic acid* (XIII),[‖] cis-*hydroxydihydro-α-campholytic acid* (XV) and *δ-keto-β-carboxy-γγ-dimethylhexoic acid* (XIV), m.p. 119–121°.[¶] If the acid is oxidised with chloric acid in the presence of osmium the *lactone* (XVI) is obtained, being formed evidently from the hydroxy-acid (XV).

---

[*] *Ber.* 1900, **33**, 2953.

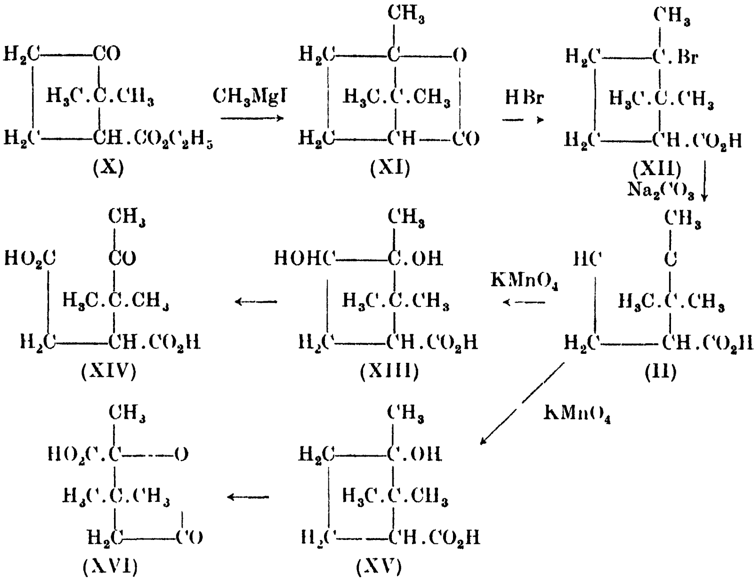
[†] The reactions of the corresponding amino-acid derived from *iso*camphoric acid have been investigated by Noyes and Littleton (*J. Amer. C.S.* 1913, **35**, 75) and by Noyes and Nickell (*ibid.* 1914, **36**, 110).

[‡] *J.C.S.* 1904, **85**, 147.

[§] Compare Noyes, *Ber.* 1895, **28**, 551.

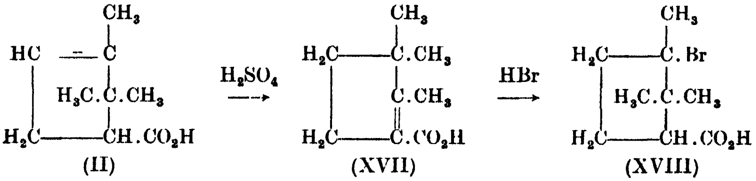
[‖] Tiemann and Kerschbaum, *Ber.* 1900, **33**, 2940; Blanc, *Bull. Soc. chim.* 1901 [iii], **25**, 83.

[¶] Chandrasena, Ingold and Thorpe, *J.C.S.* 1922, **121**, 1548; 1925, **127**, 1677.



With bromine, α-campholytic acid gives a *dibromide*, m.p. 110–114°.*

The most characteristic reaction of α-campholytic acid is the remarkable tendency which it shows to isomerise to iso*lauronolic acid* (iso*campholytic acid*, *β-campholytic acid*) (XVII), this Wagner rearrangement occurring when the acid is allowed to stand in the cold with sulphuric acid (1 : 1), or warmed with dilute sulphuric acid.† The reaction is reversible, since if *iso*lauronolic acid is treated with cold concentrated aqueous hydrogen bromide it yields the hydrobromide of α-campholytic acid (XVIII).‡



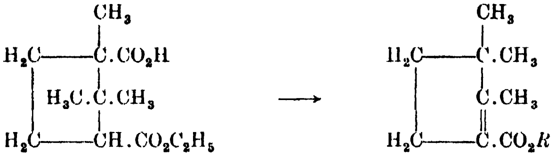
---

* Noyes, *Ber.* 1895, **28**, 552.

† Noyes, *ibid.* p. 548; *Amer. Chem. J.* 1895, **17**, 428; Perkin, *J.C.S.* 1903, **83**, 854.

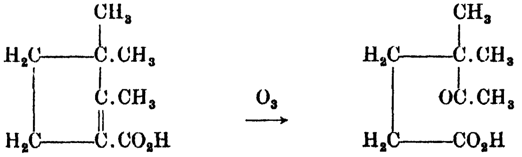
‡ Walker and Cormack, *J.C.S.* 1900, **77**, 378.

*iso*Lauronolic acid was first isolated by Walker[*] in the form of its ethyl ester from amongst the products obtained by the electrolysis of the sodium salt of α-ethyl hydrogen camphorate (XIX), and later by Walker and Cormack[†] from the corresponding methyl ester. As was mentioned on p. 494 it can be very readily prepared by the action of aluminium chloride on



(XIX) (XVII) (R = H *or* C_2H_5)

camphoric anhydride, and it is also formed when sulphocamphylic acid is distilled in superheated steam (p. 500). *iso*Lauronolic acid, which is dimorphic, melts at 135° and is volatile in steam. The constitution of the acid is established by its oxidation with ozone to (XX).[‡] This keto-acid is also obtained when chromic acid is used as the oxidising agent.[§]



(XVII) (XX)

When *iso*lauronolic acid is oxidised with potassium permanganate in ice-cold neutral solution, it behaves in a somewhat remarkable manner, the main product of the reaction being a ketonic acid, iso*lauronic* acid, m.p. 133.[‖] Blanc has shown this acid to be 1:1-*dimethyl*-Δ^3-cyclo*hexen*-2-*one*-4-*carboxylic acid* (XXII), which must be formed by the internal condensation of the diketonic acid (XXI), the reaction proceeding in accordance with the scheme:

---

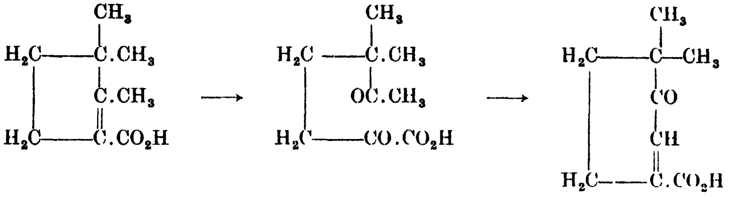
[*] *J.C.S.* 1893, **63**, 504.

[†] *Ibid.* 1900, **77**, 375.

[‡] Haworth and Perkin, *ibid.* 1908, **83**, 588.

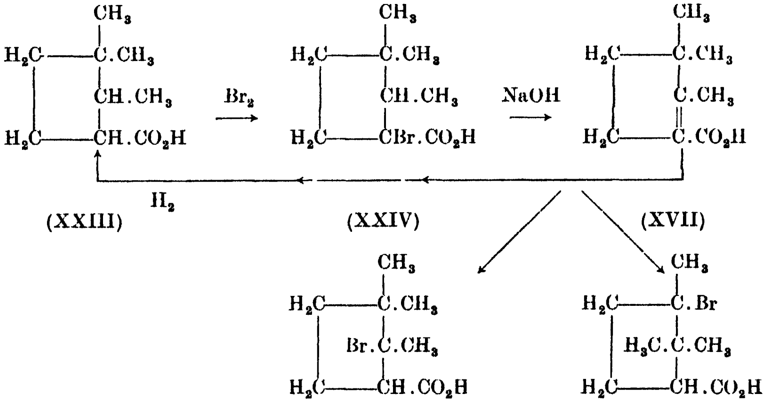
[§] Blanc, *Bull. Soc. chim.* 1898 [iii], **19**, 534; *Ann. Chim.* 1899 [vii], **18**, 259; Perkin, *J.C.S.* 1898, **73**, 844.

[‖] *Inter al.*, Blanc, *Bull. Soc. chim.* 1898 [iii], **19**, 281.



(XVII) (XXI) (XXII)

On reduction with sodium in amyl alcoholic solution *iso*lauronolic acid yields the saturated acid, *dihydroisolauronolic acid* (XXIII), b.p. 114°/22 mm.,* which gives on bromination *α-bromodihydroisolauronolic acid* (XXIV), m.p. 124–125°. This bromo-acid is reconverted into *iso*lauronolic acid by the action of alkali. The isomeric *β-bromo-acid* (XXV), m.p. 132–135°, is obtained when *iso*lauronolic acid is treated with aqueous hydrogen bromide (50 per cent.)† although, if a solution of hydrogen bromide saturated at 0° is used, then the *hydrobromide* of α-campholytic acid (XVIII) is obtained.



(XXIII) (XXIV) (XVII) (XXV) (XVIII)

When *iso*lauronolic acid is heated under pressure at 300°‡ or distilled after admixture with anthracene,§ elimination of carbon dioxide occurs with the formation of the hydrocarbon, iso*laurolene* (XXVI), b.p. 108·5°/758 mm., $d_{15}^{15°}$ 0·7867, $n_D^{20°}$ 1·4333. The constitution of this hydrocarbon has been proved by its synthesis by Blanc,[*] who also succeeded in reconverting it into

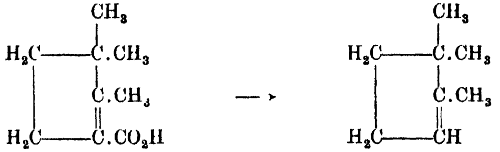
---

* Noyes, *Amer. Chem. J.* 1896, **18**, 189; Perkin, *J.C.S.* 1898, **73**, 886.

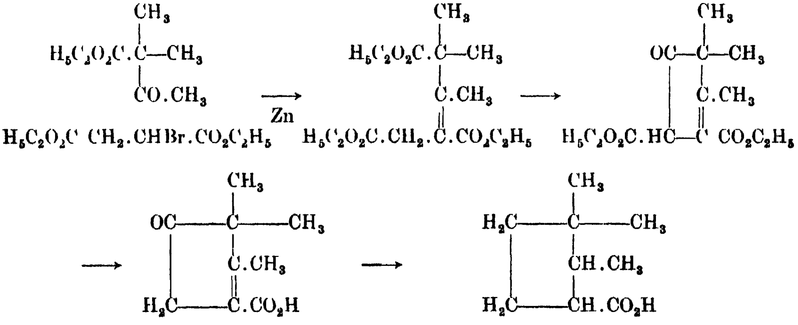
† Walker and Cormack, *J.C.S.* 1900, **77**, 381.

‡ Blanc, *Bull. Soc. chim.* 1898 [iii], **19**, 700; *Ann. Chim.* 1899 [vii], **18**, 215.

§ Crossley and Renouf, *J.C.S.* 1906, **89**, 41.


(XVII) (XXVI)

*iso*lauronolic acid, but a more direct synthesis of the acid is that described by Guha and Subramanian.[†] By the condensation of ethyl dimethylacetoacetate with ethyl α-bromosuccinate, followed by cyclisation and decarboxylation, *keto*iso*lauronolic acid* (XXVII), m.p. 186–187°, was obtained. On reduction with zinc and hydrochloric acid this gave dihydro*iso*lauronolic acid (XXIII), which was converted into *iso*lauronolic acid by bromination and treatment with alkali, as already described above.



(XXVII) (XXIII)

There has been considerable confusion in the nomenclature of the acids derived from camphoric acid by the elimination of the α- (secondary) carboxyl group, owing to the intramolecular rearrangements which occur in their formation. In the sequel Bredt's nomenclature[‡] is adopted.

---

[*] *Compt. rend.* 1906, **142,** 1085.

[†] *Ber.* 1937, **70,** 2228.

[‡] *J. pr. Chem.* 1913 [ii], **87,** 1.

Only one unsaturated acid, $C_9H_{14}O_2$, retaining the camphoric acid structure and its tertiary carboxyl group, is known. This acid, *camphonenic acid* (XXVIII), formerly designated *γ-lauronolic acid*, was first prepared in an impure state by Noyes[*] by the action of nitrous acid on *aminocamphonanic acid* (XXIX), and later by Noyes and Taveau[†] by the action of alkali on the *nitroso* derivative (XXX) of the anhydride of this acid. Camphonenic acid can be prepared most readily by the distillation of dehydrocamphoric acid (XXXI) as was mentioned on p. 496.

Camphonenic acid melts at 155–156° and its constitution has been proved by its oxidation to camphoronic acid (XXXII). Isomeric with camphonenic acid, but having a different ring structure, is the acid formerly known as *lauronolic acid*, but which has now been designated *laurolenic acid*. This acid was first prepared by Fittig and Woringer[‡] by the distillation of camphanic acid (XXXIII) and also by heating α-bromocamphoric anhydride (XXXIV) with water. It can be obtained more conveniently from the latter by warming with sodium carbonate solution.[§] It is formed also when *camphonolactone* (XXXV) is heated with hydrogen bromide and the resulting unstable *bromocamphonanic acid* (XXXVI) warmed with alkali.[||]

The identity of the acids prepared by these various methods was established by Noyes and Burke,[¶] the slight differences in their properties being due to partial racemisation. Laurolenic acid has m.p. 13°, b.p. 135–135·5°/14·5 mm., $d^{20·5}$ 1·009, $[\alpha]_D$ +185·5°, and forms a very characteristic calcium salt, which, according to Bredt,[**] crystallises with two molecules of water of crystallisation, although other authors (Noyes and Burke) state that three molecules are present. The constitution (XXXVII) now assigned to laurolenic acid, was first suggested by Lapworth,[††] who recognised that, in its preparation by any of the methods referred to above, a Wagner rearrangement, with the shift of a methyl group, occurred. The absence of the "camphoric acid" ring structure is proved by the fact that it does

---

[*] *Ber.* 1895, **28**, 553; *Amer. Chem. J.* 1894, **16**, 508; 1895, **17**, 433.

[†] *Amer. Chem. J.* 1906, **35**, 379.

[‡] *Annalen*, 1885, **227**, 1; compare Bredt and Amann, *J. pr. Chem.* 1913 [ii], **87**, 12.

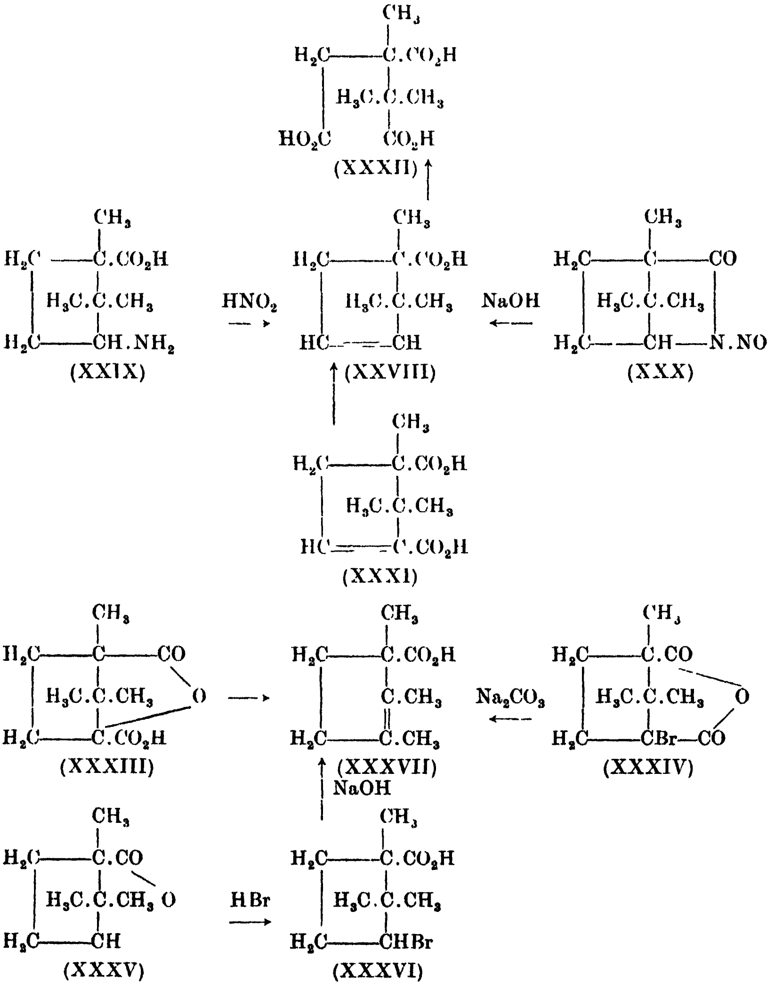
[§] Aschan, *Ber.* 1894, **27**, 3504; *Annalen*, 1896, **290**, 187; compare Tiemann and Tigges, *Ber.* 1900, **33**, 2944, Bredt, Houben and Levy, *ibid.* 1902, **35**, 1288.

[||] Bredt and Amann, *J. pr. Chem.* 1913 [ii], **87**, 12.

[¶] *J. Amer. C.S.* 1912, **34**, 174.

[**] *J. pr. Chem.* 1911 [ii], **83**, 395.

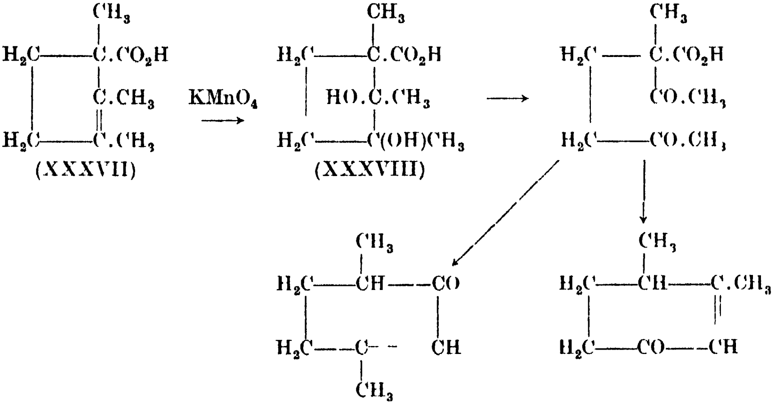
[††] *Brit. Assoc. Report*, 1900, p. 327; compare Lapworth and Lenton, *J.C.S.* 1901, **79**, 1284.



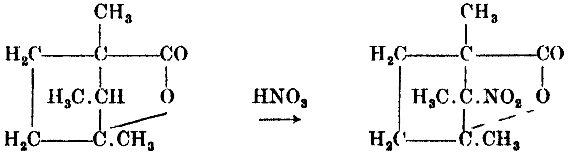
not give any camphoronic acid on oxidation.* When laurolenic acid is oxidised with potassium permanganate it yields *dihydroxydihydrolaurolenic acid* (XXXVIII), m.p. 153–154°, and *laurenone*, b.p. 92–95°/16 mm., $d^{12\cdot5^\circ}$ 0·9572, n_D 1·4853, *oxime*, m.p. 105–107°, which must be represented by either (XXXIX) or (XXXIXa).*

---

* Bredt, Houben and Levy, *Ber.* 1902, 35, 1288.


(XXXVII) (XXXVIII) (XXXIX) (XXXIXa)

When laurolenic acid is boiled with dilute acids it gives a lactone, *laurolactone*, formerly called *campholactone* (XL), m.p. 50°, which is isomeric with camphonolactone (p. 483). It was observed by Schryver† that laurolactone could be nitrated, yielding *nitrolaurolactone*, m.p. 171°, which from its reactions undoubtedly contains a tertiary nitro-group, and must therefore be represented by (XLI). Noyes and Homberger‡ prepared a structurally isomeric *nitrolactone*, m.p. 122°, by the nitration of camphonolactone.


(XL) (XLI)

With hydrogen iodide laurolenic acid gives an unstable hydriodide, which yields on reduction *laurolanic acid* (*dihydrolaurolenic acid*), b.p. 215°/749 mm., $d^{23\cdot5^\circ}$ 0·9008, n_D 1·4786, $[\alpha]_D$ + 1·74°, *amide*, m.p. 50–51°.

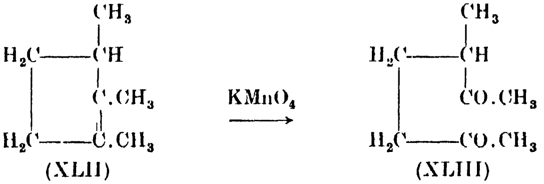
---

* Lapworth, *Brit. Assoc. Report*, 1900, p. 327; Bredt, *J. pr. Chem.* 1911 [ii], **83**, 400

† *J.C.S.* 1898, **73**, 559.

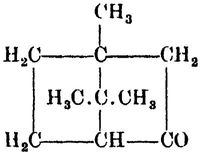
‡ *J. Amer. C.S.* 1910, **32**, 1665.

By the distillation of camphanic acid, in addition to laurolenic acid and other products, a hydrocarbon, *laurolene*, C_8H_{14}, is formed.[*] Laurolene is also obtained when calcium camphanate is distilled,[†] by the distillation of laurolenic acid,[‡] by the action of sodium nitrite on aminolauronic acid or by the action of alkali on the nitroso derivative of aminolauronic anhydride.[§] Laurolene, prepared by any of these methods, has b.p. 119·5–120·5°/760 mm., $d_{10}^{10°}$ 0·8048, n_D 1·4437, the rotatory power showing marked variations, $[\alpha]_D$ $+28·65°$ to $-14·7°$. It was suggested by Eykman[||] that it was probably represented by (XLII), and support was lent to this structure by the observation of Noyes and Derick that, on oxidation with potassium permanganate, *αγ-diacetylbutane* (XLIII) was obtained. This constitution was confirmed by Noyes and Kyriakides,[¶] who described a synthesis of the hydrocarbon.



(XLII) (XLIII)

EPICAMPHOR (*β-CAMPHOR*)



Although epicamphor (or β-camphor) (I) has not been found to occur in nature, in view of its close structural relationship to camphor (II) it was generally recognised that a study of its reactions was likely to be of considerable interest and might assist in the solution of a number of difficult problems connected with the chemistry of camphor and its derivatives. Many unsuccessful attempts at its preparation are recorded in the literature,[*] whilst Wagner[†] considered that the hydration of bornylene (III) by the Bertram-Walbaum process gave epiborneol (IV) as its acetate which on hydrolysis and oxidation yielded epicamphor.

---

[*] Aschan, *Annalen*, 1896, **290**, 187; compare Crossley and Renouf, *J.C.S.* 1906, **89**, 37.

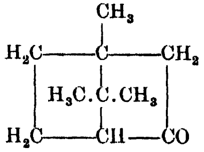
[†] Wreden, *Annalen*, 1872, **163**, 337; compare Rupe and Maull, *Ber.* 1893, **26**, 1202.

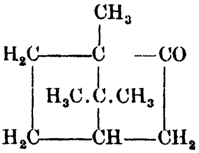
[‡] Walker and Henderson, *J.C.S.* 1896, **69**, 749.

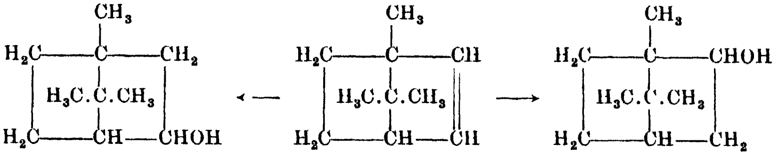
[§] Noyes, *Amer. Chem. J.* 1894, **16**, 508; 1895, **17**, 432; Noyes and Derick, *J. Amer. C.S.* 1909, **31**, 671; 1910, **32**, 1061.

[||] *Chem. Weekblad*, 1906, **4**, 50.

[¶] *J. Amer. C.S.* 1910, **32**, 1064.


(I)


(II)


(IV) (III) (V)

Bredt and Hilbing[‡] found, however, that the hydration of bornylene yields an acetate which gives on hydrolysis a mixture of alcohols, which consist essentially of borneol and *iso*borneol (V), since on oxidation only camphor is obtained. It is of course not impossible that epiborneol is also formed to a slight extent.[§]

l-Epicamphor was first prepared by Lankshear and Perkin[‖] from d-*camphane*-3-*carboxylic acid* (VI), an acid which can be prepared from *d*-camphor-3-carboxylic acid[¶] (see p. 451). By the bromination of the acid chloride of this acid the *bromo*-acid (VII) was obtained and from this, by the action of potassium acetate and alcoholic potassium hydroxide, the *hydroxy* acid (VIII). When this acid was oxidised with either chromic acid, lead peroxide or potassium permanganate, *l*-epicamphor (I) was formed.

---

[*] Duden and Macintyre, *Annalen*, 1900, **313**, 59; Haller and Blanc, *Compt. rend.* 1905, **141**, 697.

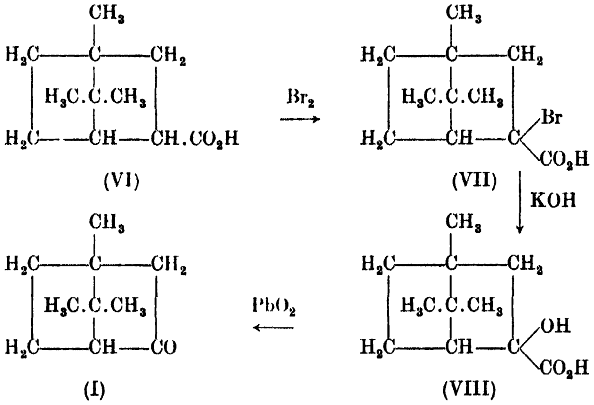
[†] *Chem.-Ztg.* 1903, **27**, 271; *Ber.* 1903, **36**, 4602.

[‡] *J. pr. Chem.* 1911 [ii], **84**, 783.

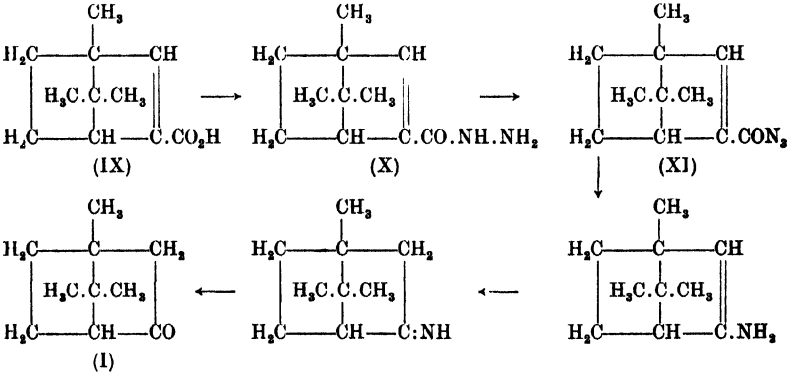
[§] Compare Schavrigin and Prostakov, *Chem. Abs.* 1948, p. 7276.

[‖] *Proc. C.S.* 1911, **27**, 167.

[¶] Bredt, *Annalen*, 1906, **348**, 200; 1909, **366**, 1.



A few months later Bredt and Hilbing* prepared *l*-epicamphor by a somewhat different process. They converted d-*bornylene*-3-*carboxylic acid* (IX) through its acid chloride into the *hydrazide* (X), from which by the Curtius method the *azide* (XI) was prepared; on digestion with hydrochloric acid this gave *l*-epicamphor.

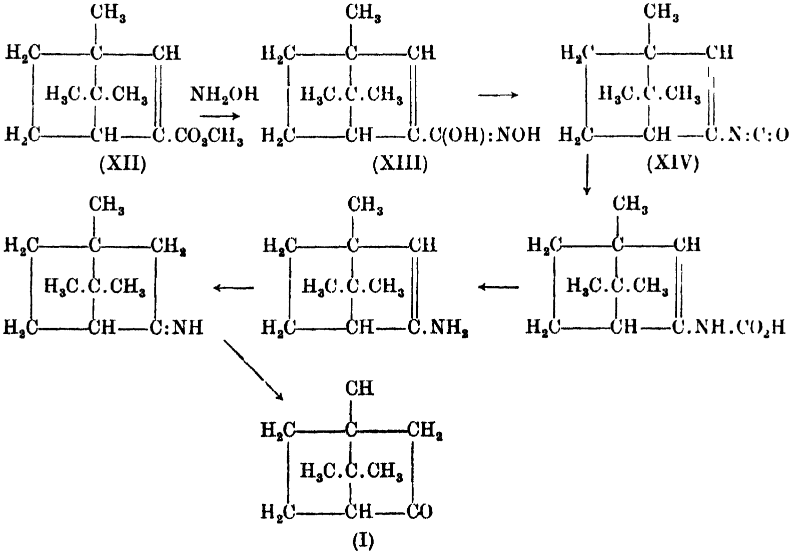


Bredt and Perkin joined forces in investigating the chemistry of *l*-epicamphor and two years later† gave an account of their work. They found that neither of the methods referred to above was suitable for the preparation of the ketone, since, although the latter method was preferable, it suffered from the disadvantage that the azide (XI) was explosive, and hence it was only possible to work with small quantities of material. A new process was therefore devised starting from d-*bornylene*-3-*hydroxamic acid* (XIII), m.p. 136°, which was readily obtained by the action of hydroxylamine on *methyl* d-*bornylene*-3-*carboxylate* (XII) in the presence of sodium methoxide.* This acid passed, on heating above its melting-point, with extreme ease into *l*-epicamphor, due doubtless to the fact that it isomerises to d-*bornylene*-3-iso*cyanate* (XIV), which is decomposed by the water formed in the reaction to yield *l*-epicamphor and ammonia. At the same time a considerable quantity of resin, *d*-bornylene-3-*iso*cyanate, is obtained which can be hydrolysed by hydrochloric acid to *l*-epicamphor.

---

* *Chem.-Ztg.* 1911, **35**, 765.

† *J.C.S.* 1913, **103**, 2182.

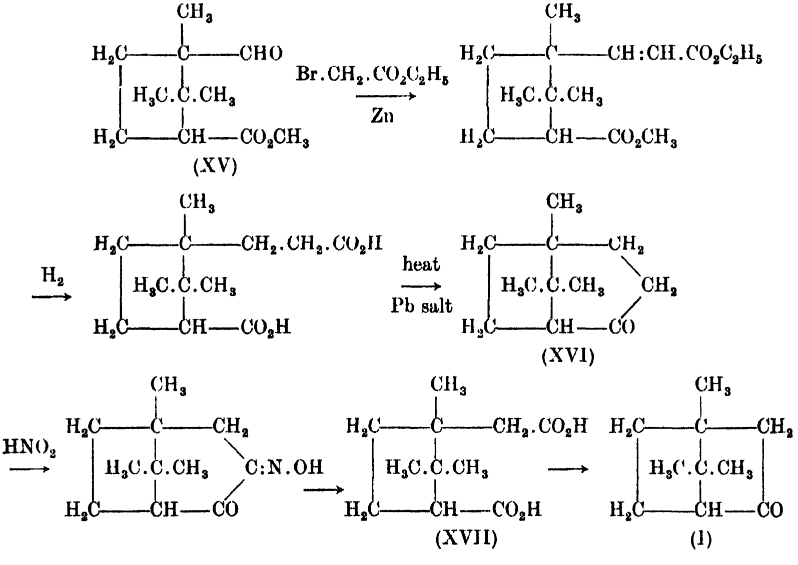


The intramolecular change, (XIII) to (XIV), can be carried out very smoothly by shaking the sodium salt of the hydroxamic acid with *p*-toluenesulphonyl chloride, the *iso*cyanate being then hydrolysed with hydrochloric acid. Starting from *l*-camphor Furness and Perkin[*] prepared *d*-epicamphor by the same series of reactions. Epicamphor can probably be most conveniently prepared in quantity, however, by the reduction of "β-hydroxy camphor" (2-hydroxyepicamphor) with sodium amalgam[†] (see p. 428).

---

* Compare Lossen, *Annalen*, 1875, **175**, 313; **178**, 213; Thiele and Pickard, *ibid.* 1899, **309**, 189.

Epicamphor has also been prepared by several other methods. Salmon-Legagneur,[‡] starting from the methyl ester of camphoric acid *tert.*-semialdehyde (XV) (p. 471), obtained *β-homocamphor* (homoepicamphor) (XVI), m.p. 202–204°, $[\alpha]^{13^\circ}_{D}$ $+111{\cdot}2^\circ$, and converted this, through *β-homocamphoric acid* (XVII), into *l*-epicamphor, the reactions involved being shown in the scheme below:



Asahina and Ishidate[§] treated 2:5-*diketocamphane* (XVIII) with hydrogen cyanide and hydrolysed the resulting hydroxynitrile to a mixture of stereoisomeric forms of 5-*hydroxycamphor-5-carboxylic acid* (XIX), α-, m.p. 151–152°, $[\alpha]^{17^\circ}_{D}$ $-6{\cdot}5^\circ$ (*amide*, m.p. 248–249°), and β-, m.p. 153°, $[\alpha]_D^{17^\circ}$ $+21{\cdot}6^\circ$ (*amide*, m.p. 190–191°). Reduction of the *semicarbazones* (m.p.'s 267° and 225° respectively) with sodium ethoxide gave α- (m.p. 151°) and β- (m.p. 130°) 3-*hydroxycamphane*-3-*carboxylic acid* (XX), both of which on oxidation with chromic acid gave *d*-epicamphor (I).

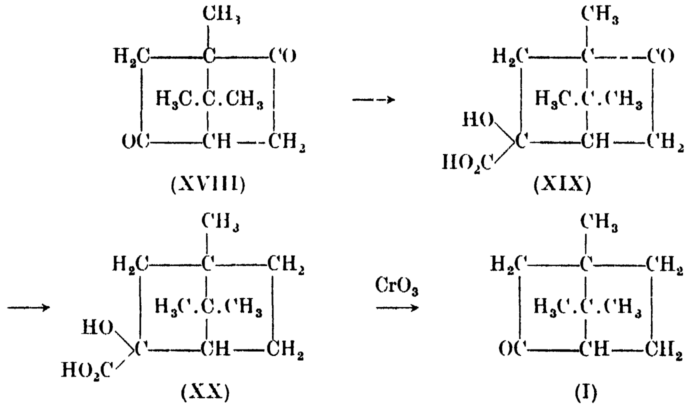
---

[*] *J.C.S.* 1914, **105**, 2024.

[†] Bredt and Bredt-Savelsberg, *Ber.* 1929, **62**, 2216.

[‡] *Compt. rend.* 1931, **192**, 748; 1932, **194**, 467; *Bull. Soc. chim.* 1932 [iv], **51**, 807.

[§] *Ber.* 1933, **66**, 1913.



(XVIII) (XIX) (XX) (I)

dl-Epicamphor and a number of its derivatives have been prepared by Bredt, Drouven, Schumann and Scholl[*] from *dl*-bornylene-3-carboxylic acid (compare p. 514). The *dl*-ketone has also been obtained by the oxidation of synthetic *dl*-epiborneol (see below).

Epicamphor has an odour very similar to, yet distinct from, that of camphor. The *d*- and *l*-forms melt at 182° and the *dl*-form at practically the same temperature, 180°; it boils at 213°, $[\alpha]_D$ $+58{\cdot}4^\circ$, $-58{\cdot}2^\circ$ (in benzene). The ketone can be characterised by the preparation of the *oxime*,[†] *d*- and *l*-, m.p. 103–104°, $[\alpha]_D$ $+98{\cdot}9^\circ$, $-100{\cdot}5^\circ$ (in benzene), *dl*-, m.p. 99–100°, or the *semicarbazone*, *d*- and *l*-, m.p. 237–238°.

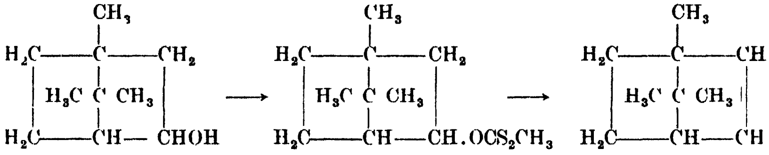
On reduction with sodium and alcohol *l*-epicamphor yields l-*epiborneol* (IV), m.p. 181–182·5°, *phenylurethane*, m.p. 82°. No evidence was obtained of the formation of a stereoisomeric alcohol corresponding to *iso*borneol, but according to Lipp and Bund[‡] the hydrogenation of epicamphor over a platinum catalyst gives iso*epiborneol*, m.p. 194·5°, $[\alpha]_D^{30}$ +13·2° (in toluene), *phenylurethane*, m.p. 94–98°, 3:5-*dinitrobenzoate*, m.p. 120°. When heated with sodium it isomerises to epiborneol. It is of interest to note that *l*-epiborneol prepared from *l*-epicamphor appeared to be optically inactive, but this optical inactivity was only apparent, since, when the alcohol was converted into *methyl* l-*epibornylxanthate* (XXI) by Tschugaev's method and this ester distilled, l-*bornylene* (III), $[\alpha]_D$ −18·4° (in benzene), was obtained, and this gave *d*-camphoric acid on oxidation. According to Asahina and Ishidate,[*] *l*-epiborneol, prepared by reduction of the semicarbazone of 5-hydroxycamphor (p. 429), has m.p. 188°, $[\alpha]_D^{17°}$ −3·4° (in alcohol).

---

[*] *J. pr. Chem.* 1931 [ii], **131**, 132.

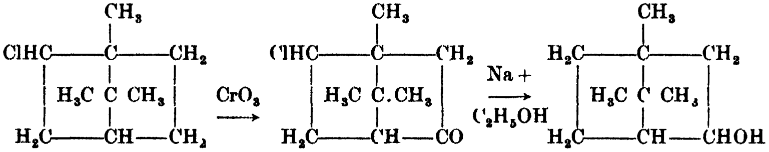
[†] The oxime prepared from *l*-epicamphor is dextrorotatory, a reversal of sign occurring, as in the case of camphor.

[‡] *Ber.* 1935, **68**, 249; compare Lipp, Oeckinghaus and Conze, *ibid.* 1941, **74**, 6.



(IV) (XXI) (III)

l-Epiborneol has also been prepared by Bredt and Pinten[†] from bornyl chloride (XXI), which on oxidation with chromic acid gives 6-*chloroepicamphor* (XXII), m.p. 161°, and this on reduction with sodium and alcohol yields *l*-epiborneol. Reference has already been made (p. 358) to the synthesis of *dl*-epiborneol (3.5-*dinitrobenzoate*, m.p. 105°) by the diene condensation; on oxidation it gives *dl*-epicamphor, thus constituting a synthesis of the latter compound.



(XXI) (XXII) (IV)

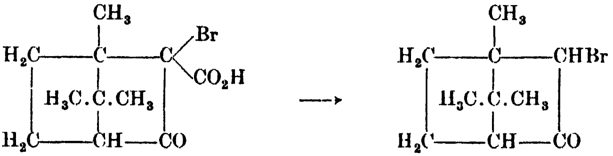
l-Epicamphor is comparatively stable to oxidising agents and is scarcely attacked by cold dilute potassium permanganate; it can, however, be oxidised by nitric acid (d = 1·3) at 100°, when it yields *d*-camphoric acid.

---

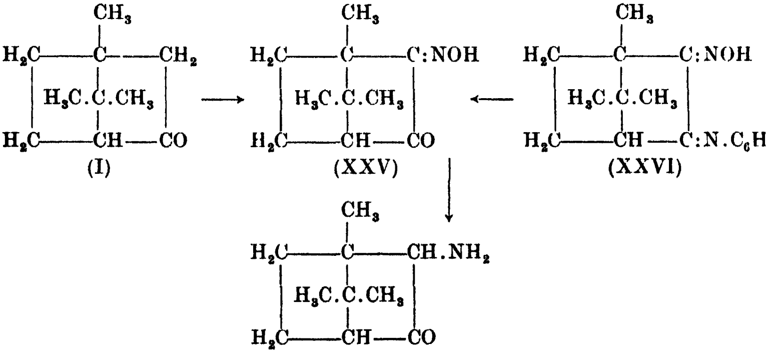
[*] *Ber.* 1934, 67, 71

[†] *J. pr. Chem.* 1927 [ii], 115, 45; compare Murayama and Anhara, *J. Pharm. Soc. Japan*, 1926, no. 528, 14.

Bromo-l-*epicamphor* (XXIII), m.p. 133–134°, $[\alpha]_D$ $-86{\cdot}6°$ (in ethyl acetate), can be readily prepared by the action of bromine on *l*-epicamphor at 100°. The *dl*-modification melts at 135°. Bromo-*l*-epicamphor is also obtained when *bromo*-l-*epicamphor*-2-*carboxylic acid* (XXIV) (see p. 520) is heated above its melting-point. Its constitution is therefore proved. A second unstable modification has been described by Bredt.* It melts at 144° and on standing passes into the stable form, m.p. 134°.


(XXIV) (XXIII)

Like camphor (see p. 466), *l*-epicamphor reacts readily with *iso*amyl nitrite in the presence of sodamide to yield iso*nitroso*-l-*epicamphor* (XXV), which is obtained in two modifications, α-, m.p. 168–170°, $[\alpha]_D$ $-201{\cdot}9°$ (in benzene), β-, m.p. 138–140°, $[\alpha]_D$ $-183{\cdot}5°$ (in benzene). The latter isomeride is unstable and on boiling with water gives the α-modification. These two *iso*-nitroso-*l*-epicamphors have also been prepared by Foster and Spinner† by the hydrolysis of the two oximes of phenyliminocamphor (XXVI) (see p. 475).


(I) (XXV) (XXVI) (XXVII)

Both forms of *iso*nitroso-epicamphor yield, on hydrolysis with hydrochloric acid and formaldehyde, camphorquinone, and with sulphuric acid, *d*-camphorimide; on reduction with zinc dust and sodium hydroxide they yield the same *amino*-l-*epicamphor* (XXVII), m.p. 168–170°, $[\alpha]_D$ +15° (in benzene). Amino-*l*-epicamphor, unlike α-aminocamphor,[*] is comparatively stable.

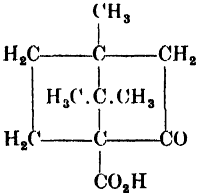
---

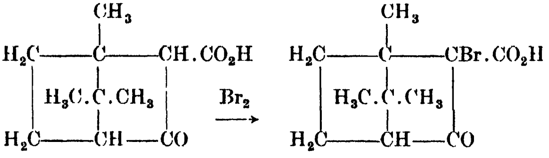
* *J. pr. Chem.* 1931 [ii], **131**, 135.

† *J.C.S.* 1912 **101**, 1348.

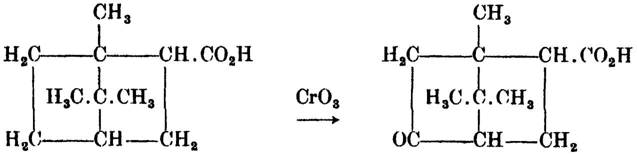
Like camphor, *l*-epicamphor does not react with hydrogen cyanide, which is somewhat remarkable, since, unlike camphor, the keto group is not adjacent to a tertiary carbon atom.

l-*Epicamphor*-2-*carboxylic acid* (XXVIII), m.p. 120–122°, $[\alpha]_D$ −18·5° (in ethyl acetate), can be readily prepared by boiling a benzene solution of the ketone with sodamide in a current of carbon dioxide. Since its alcoholic solution gives with ferric chloride a green coloration, and it can be readily brominated to give α-*bromo*-l-*epicamphor*-2-*carboxylic acid* (XXIX), m.p. 145°, it follows that the acid must be represented by (XXVIII) and not by the alternative formula (XXVIIIa).


(XXVIIIa)


(XXVIII) (XXIX)

An isomeric acid, m.p. 185°, $[\alpha]_D$ ± 0°, has been prepared by Murayama and Tanaka[†] by the oxidation of *camphane*-2-*carboxylic acid* (XXX) with chromic acid. This acid is considered to be *epicamphor*-6-*carboxylic acid* (XXXI).


(XXX) (XXXI)

l-Epicamphor-2-carboxylic acid cannot be reduced with sodium amalgam, but on electrolytic reduction it yields l-*epi*-*borneol*-2-*carboxylic acid* (XXXII), which has been obtained in four modifications:[‡] A, m.p. 125°, $[\alpha]_D$ +2·36°; B, m.p. 145°,

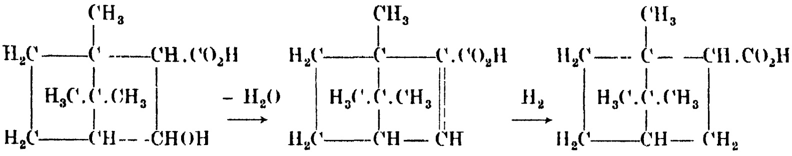
---

[*] Duden and Pritzkov, *Annalen*, 1899, **307**, 209.

[†] *J. Pharm. Soc. Japan*, 1926, **527**, 1.

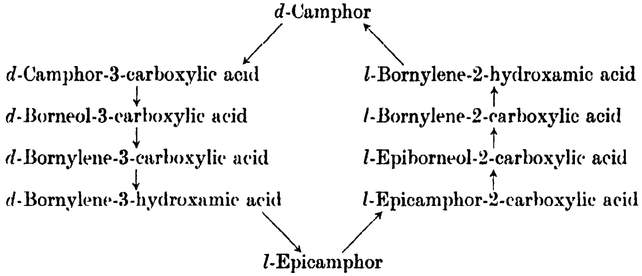
[‡] All the determinations of rotatory power were made in ethyl acetate solution.

$[\alpha]_D$ −4·8°; C, m.p. 173°, $[\alpha]_D$ +15·18°; and D, m.p. 237°, $[\alpha]_D$ +77·9°. When the hydroxy acid is heated with acetyl chloride, elimination of water occurs with the formation of l-*bornylene-2-carboxylic acid* (XXXIII), m.p. 115°, $[\alpha]_D$ −98·82° (in ethyl acetate). This acid gives on reduction l-*camphane-2-carboxylic acid* (XXX), m.p. 78–80°, $[\alpha]_D$ −37·8° (in ethyl acetate).



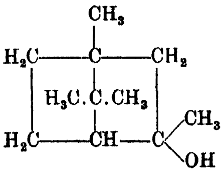
(XXXII) (XXXIII) (XXX)

l-Bornylene-2-carboxylic acid can be converted into *d*-camphor in exactly the same manner as *d*-bornylene-3-carboxylic acid is converted into *l*-epicamphor. The reactions involved in this interesting cycle are shown in the scheme:

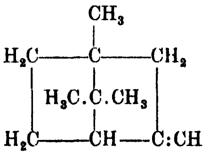


d-Camphor
d-Camphor-3-carboxylic acid
d-Borneol-3-carboxylic acid
d-Bornylene-3-carboxylic acid
d-Bornylene-3-hydroxamic acid
l-Bornylene-2-hydroxamic acid
l-Bornylene-2-carboxylic acid
l-Epiborneol-2-carboxylic acid
l-Epicamphor-2-carboxylic acid
l-Epicamphor

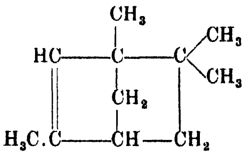
dl-Epicamphor reacts with methyl magnesium iodide to give 3-*methylepiborneol* (XXXIV), m.p. 59–60°, which on dehydration gives a mixture of 4-*methyl-α-fenchene* (XXXV) and, probably, 4-*methyl-γ-fenchene* (XXXVI).*



(XXXIV)



(XXXV)



(XXXVI)

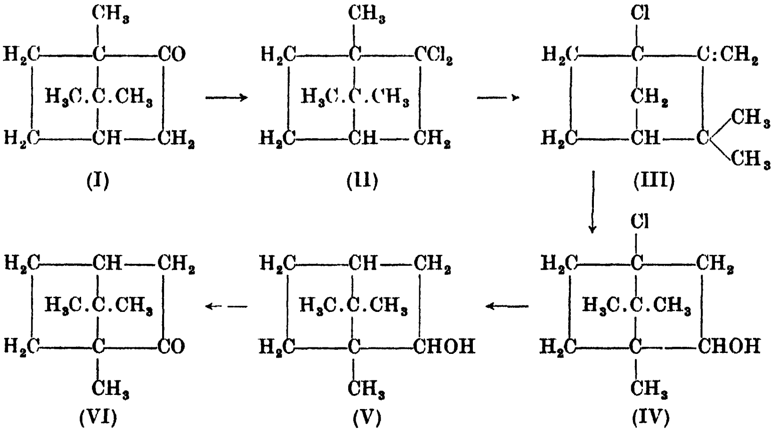
---

* Nyman and Kuvaja, *Annalen*, 1939, **538**, 68.

INTERCONVERSION OF ENANTIOMORPHS IN THE CAMPHOR SERIES

Reference has already been made (p. 163) to the fact that an isomerisation of the Nametkin type may lead to an inversion of configuration, thus accounting, for example, for certain racemisation phenomena. By an extension of these reactions it has been possible to convert *d*- into *l*-, and *l*- into *d*-camphor, and also to bring about similar interconversions with certain derivatives of camphor. The brief account which follows is taken from the experiments of Houben and Pfankuch;* for full details of the many ramifications of the work, the original papers should be consulted.

l-*Camphor* (I), $[\alpha]_D$ $-43°$, was converted with phosphorus pentachloride into the dextro-rotatory α-dichloride (II), $[\alpha]_D$ $+15{\cdot}2°$, from which *α-chlorocamphene* (III), $[\alpha]_D$ $+18{\cdot}8°$ was obtained by elimination of hydrogen chloride with potassium acetate. When this was treated with trichloroacetic acid it underwent both the Nametkin and Wagner transformations, to give, after saponification, 4-*chloro*iso*borneol* (IV), $[\alpha]_D$ $-23°$, which on reduction with sodium and alcohol furnished l-iso*borneol* (V), $[\alpha]_D^{20°}$ $-23{\cdot}7°$, oxidised by chromic acid to d-*camphor* (VI), m.p.

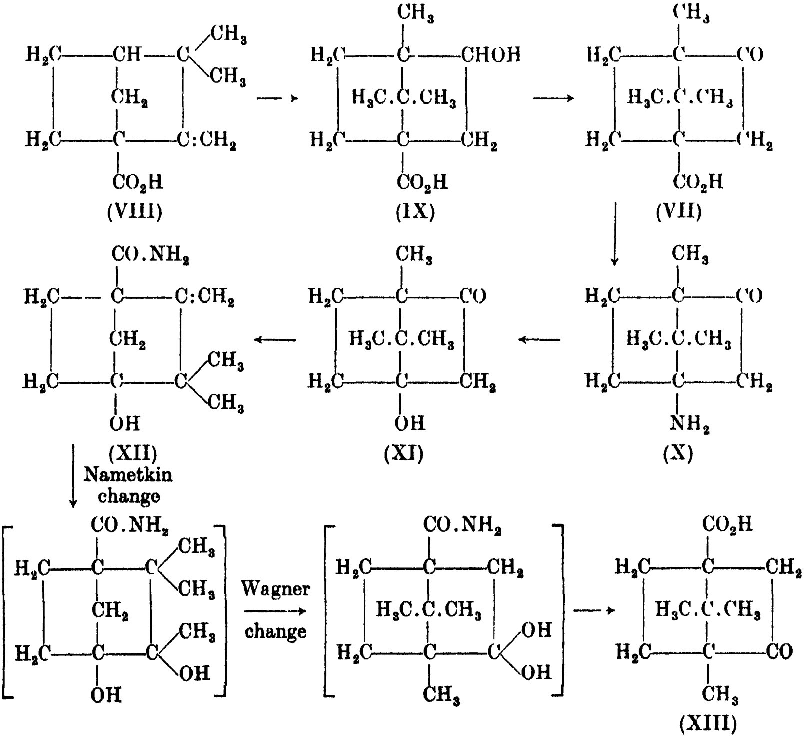


---

* *Annalen*, 1930, **483**, 271; 1931, **489**, 193; 1933, **501**, 219; *Ber.* 1931, **64**, 2719.

172°, $[\alpha]_D$ +32° (in alcohol). This represents an "optical conversion" of 74 per cent., the remainder having been racemised. The tendency for racemisation can be diminished by the use of hydrogen bromide instead of trichloroacetic acid, when 4-chloro-*iso*bornyl bromide, m.p. 156–158°, is obtained as an intermediate product. An alternative method for the conversion of (IV) to (VI) is to carry out the oxidation first, to give 4-*chlorocamphor*, which is then reduced to camphor, preferably through the semicarbazone, with sodium and alcohol. This was the method adopted to convert *d*-camphor ($[\alpha]_D$ +45°) into *l*-camphor ($[\alpha]_D$ −29°), the intermediate 4-chlorocamphor having m.p. 198–199°, $[\alpha]_D^{20^\circ}$ −30°.

As a further example, the transformation of l-*camphor*-4-*carboxylic acid* (VII) into its enantiomorph will be considered. This acid, m.p. 238–240°, $[\alpha]_D^{20^\circ}$ −19·5° (formerly considered to be the 6-derivative), is obtained from d-*camphene*-1-*carboxylic*



acid (VIII) (compare p. 344) by hydration with trichloroacetic acid to d-*borneol*-4-*carboxylic acid* (IX), followed by oxidation with chromic acid. It was converted through the acid chloride into the *amide*, m.p. 207–208°, and thence into 4-*aminocamphor* (X), m.p. 230–232°, the structure of which was confirmed by treatment with nitrosyl chloride in the presence of copper carbonate, when it gave 4-chlorocamphor, m.p. 198–199°, identical with that referred to above. By the action of nitrous acid on the amine, 4-*hydroxycamphor* (XI), m.p. 250°, $[\alpha]_D$ $-16°$, was prepared, the *oxime* (m.p. 212°) of which, on treatment with nitrous acid, followed by potassium cyanide,* gave the *amide* of 4-*hydroxycamphene*-1-*carboxylic acid* (XII), m.p. 201–203°, $[\alpha]_D$ $-28{\cdot}5°$. When this was hydrolysed with concentrated hydrochloric acid it underwent the Nametkin and Wagner rearrangements, and d-*camphor*-4-*carboxylic acid* (XIII) was obtained; the product had m.p. 238–240°, $[\alpha]_D^{18°}$ $+18{\cdot}5°$, representing an "optical conversion" of 95 per cent.

An entirely different principle, not dependent upon any molecular rearrangement, has been applied by Asahina, Ishidate and Momose† to the conversion of *d*- into *l*-camphor. By the oxidation of *d*-camphor (XIV) with chromic acid, d-p-*diketocamphane* (XV) may be obtained. This was converted, as shown in the scheme below,‡ into d-*epicamphor* (XVI), which when oxidised with selenium dioxide gave d-*camphorquinone* (XVII), $[\alpha]_D$ $+100{\cdot}1°$, the enantiomorph of the diketone obtained by the usual methods from *d*-camphor (compare p. 466). When reduced by zinc and acetic acid it gave a mixture of l-3-*hydroxycamphor* (XVIII), m.p. 192–195°, $[\alpha]_D^{25°}$ $-13{\cdot}8°$, and l-2-*hydroxyepicamphor* (XIX), m.p. 214°, $[\alpha]_D^{23°}$ $-10°$, which, after separation, were reduced by sodium amalgam to l-*camphor* (XX), m.p. 176°, $[\alpha]_D^{26°}$ $-41{\cdot}4°$, and *d*-epicamphor (XVI), respectively.

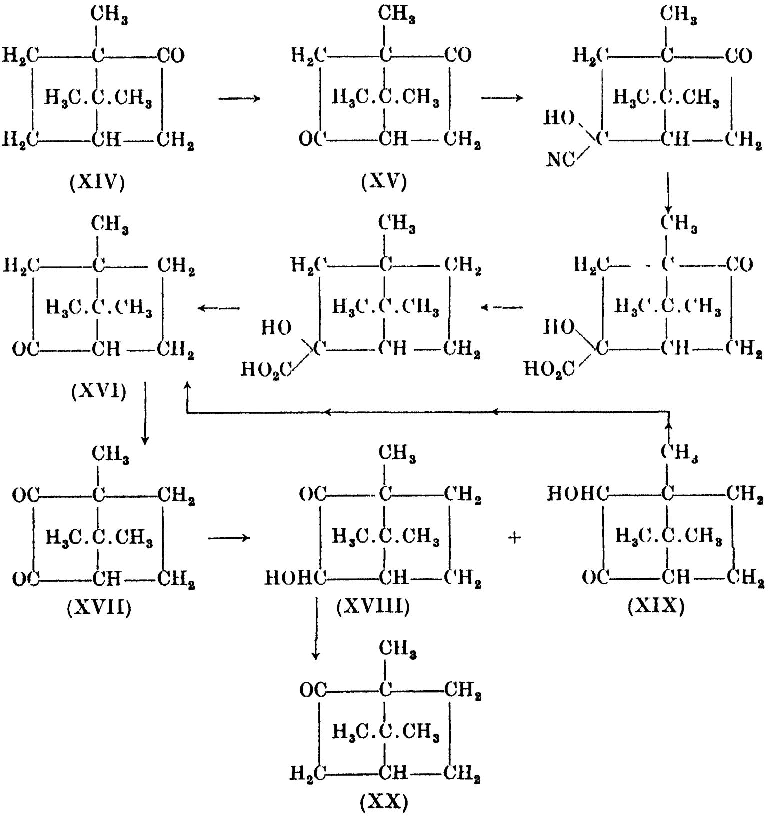
It is clear that the interconversion of *d*- and *l*-epicamphor could also be brought about by application of the above reactions in conjunction with those discussed on p. 521 for the conversion of *l*-epicamphor into *d*-camphor.

---

* The reactions involved at this stage are similar to those which occur in the preparation of camphene-1-carboxylic acid from camphor, *via* pernitrosocamphor (p. 441).

† *Ber.* 1933, **66**, 1913; 1934, **67**, 1432.

‡ These reactions have been considered in more detail on p. 516.



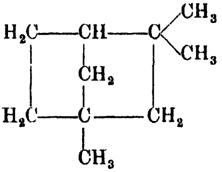
(XIV) (XV) (XVI) (XVII) (XVIII) (XIX) (XX)

CHAPTER VI

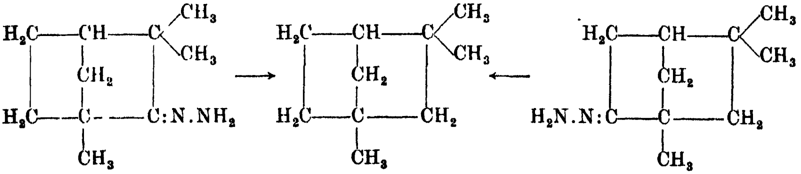
FENCHANE, *ISO*BORNYLANE AND THEIR DERIVATIVES

A. HYDROCARBONS

FENCHANE



Fenchane (II), the parent hydrocarbon of the important ketone, fenchone, was prepared in 1911 simultaneously by Wolff[*] by the action of sodium ethoxide on d-*fenchonehydrazone* (I) and by Kishner[†] by distillation of this substance with potassium hydroxide. More recently it has been obtained by treatment of dl-iso*fenchonehydrazone* (III) with sodium ethoxide.[‡]



(I) (II) (III)

Direct proof that fenchane contains the same ring structure as fenchone and that no molecular rearrangement has taken place was furnished by Nametkin's investigation[§] of the action of nitric acid on the hydrocarbon. When fenchane is heated with dilute nitric acid at 135–140° it yields a mixture of two secondary nitrofenchanes, b.p. 139–140°/40 mm., which cannot be separated from one another. These must be 2-*nitrofenchane* (IV) and 6-*nitrofenchane* (V), since on oxidation with potassium permanganate a mixture of *fenchone* (VI) and iso*fenchone* (VII) is obtained. An additional product of the action of nitric acid is iso*fenchocamphoric acid* (VIII), which evidently results from the degradation of *iso*fenchone.

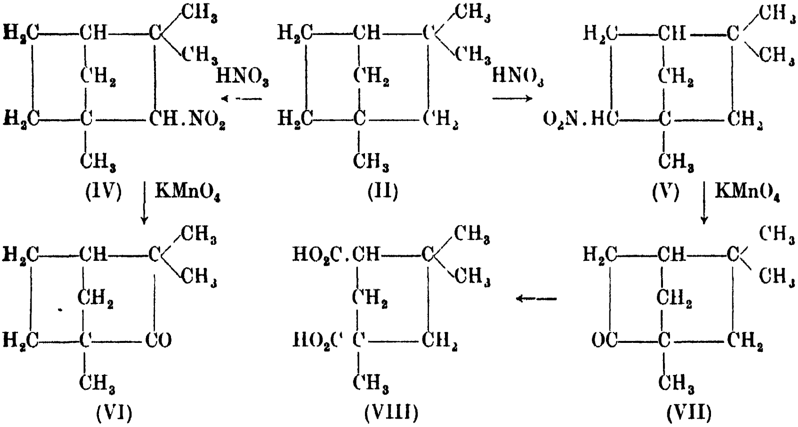
---

[*] *Annalen*, 1911, **394**, 97.

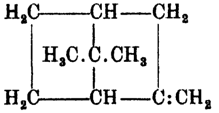
[†] *J. Russ. Phys. Chem. Soc.* 1912, **43**, 584.

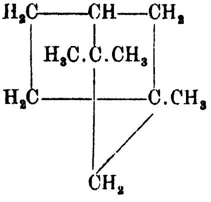
[‡] Komppa and Hasselström, *Annalen*, 1932, **496**, 164.

[§] *J. Russ. Phys. Chem. Soc.* 1915, **47**, 1590.



Fenchane has also been obtained by Qvist* by the reduction of α-fenchene dibromide (p. 542) with sodium and alcohol, when a mixture of α-fenchene (IX) and fenchane (II) is obtained. The constitution of the dibromide is not known, but the reaction, like that of the conversion of camphene dibromide into tricyclene and camphene,† must involve a Wagner rearrangement.


(IX)


(II)

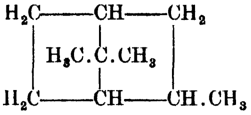
Fenchane, prepared from *d*-fenchonehydrazone, does not solidify when cooled to −15° and, according to Wolff, boils at 149°/750 mm., $d_{4^\circ}^{20^\circ}$ 0·8316, $n_D^{20^\circ}$ 1·4412, $[\alpha]_D$ −18·11°, values in very close agreement with those observed by Kishner. The *dl*-hydrocarbon boils at 151–152°/760 mm.

---

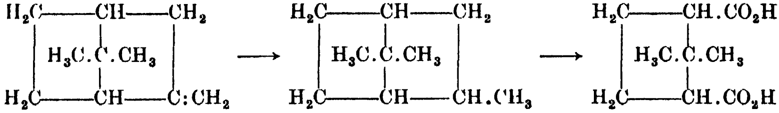
* *Annalen*, 1918, **417**, 293.

† Godlewski, *J. Russ. Phys. Chem. Soc.* 1905, **37**, 459.

ISO*BORNYLANE*[*]

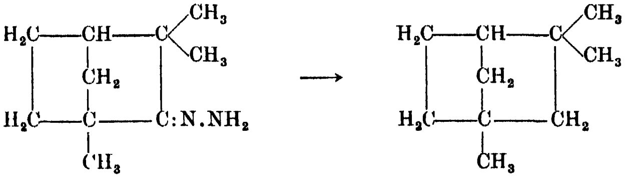


By the catalytic hydrogenation of α-fenchene (I) by the Sabatier-Senderens method, Zelinski[†] prepared a saturated hydrocarbon, $C_{10}H_{18}$, to which he gave the name fenchane and which he represented by (II), since it gave on oxidation cis-*apocamphoric acid* (III).



(I) (II) (III)

In 1911 Wolff[‡] and Kishner[§] prepared from *fenchonehydrazone* (IV) an isomeric hydrocarbon (V) having completely different properties. Following the analogy of the nomenclature adopted in the camphane series, this hydrocarbon was designated *fenchane*, whilst for Zelinski's hydrocarbon the name iso*bornylane* was adopted.



(IV) (V)

*iso*Bornylane has been studied by Nametkin,[||] who has shown that it can also be prepared by the catalytic hydrogenation of *fenchone* (VI) using the Sabatier-Senderens method. This reduction involves a Wagner rearrangement.

---

[*] *iso*Bornylane is also termed *α-fenchane*.

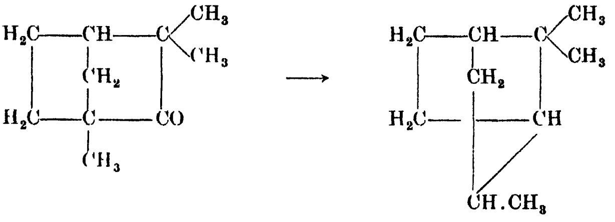
[†] *J. Russ. Phys. Chem. Soc.* 1904, **36**, 770.

[‡] *Annalen*, 1912, **394**, 97.

[§] *J. Russ. Phys. Chem. Soc.* 1911, **43**, 582.

[||] *Ibid.* 1915, **47**, 1590; *Annalen*, 1924, **440**, 60.

Ipatiev[*] has also prepared *iso*bornylane from fenchone and from fenchyl alcohol by hydrogenation over a mixed nickel oxide-aluminium oxide catalyst, whilst Zelinski and Lewina[†] have shown it to be formed when *cyclo*fenchene (p. 551) is distilled over platinum black in a current of hydrogen at 155–160°.


(VI) (II)

*iso*Bornylane is an oil, b.p. 163·5-164·5°/753 mm., $d_{4°}^{20°}$ 0·8566, $n_D^{20°}$ 1·4577. The pure dextro- and laevorotatory forms have not been described, the hydrocarbon prepared by Zelinski being laevorotatory, $[\alpha]_D$ $-8{\cdot}16°$, whilst Ipatiev gives the value $[\alpha]_D$ $-19{\cdot}83°$. For *dl-iso*bornylane, prepared by the hydrogenation of *dl*-α-fenchene over a palladium catalyst, Komppa and Beckmann[‡] found b.p. 161-163°, d_4^{20} 0·8612, n_D^{20} 1·4615.

When *iso*bornylane is heated with dilute nitric acid ($d = 1{\cdot}075$) at 130–135° it behaves differently from fenchane (compare p. 526) and yields, as the main product of the reaction, a tertiary *nitro*-derivative, m.p. 57–58°,[§] b.p. 112–113°/12 mm., $d_4^{20°}$ 1·0575, $n_D^{20°}$ 1·4813, together with *cis*-apocamphoric acid and a second nitro-derivative, which is described below.

The formation of a tertiary nitro-derivative is direct evidence of the presence in *iso*bornylane of the grouping $>CH.CH_3$, and there can be no doubt that this substance is represented by (VII). On reduction it yields the corresponding *amine* (VIII), m.p. 26–27·5°, b.p. 199–199·5°/756 mm., $d_{4°}^{20°}$ 0·9171, $n_D^{20°}$ 1·480 (*benzoyl* derivative, m.p. 155°), and from this, by the action of nitrous acid, the alcohol, iso*bornylol* (IX), m.p. 46–48°, can be prepared. This alcohol is probably identical with *methyl-α-fenchocamphorol,* prepared by Komppa and Roschier[*] from *α-fenchocamphorone* (X), and which they found to give *dl*-α-fenchene on distillation at ordinary pressure (compare p. 539).

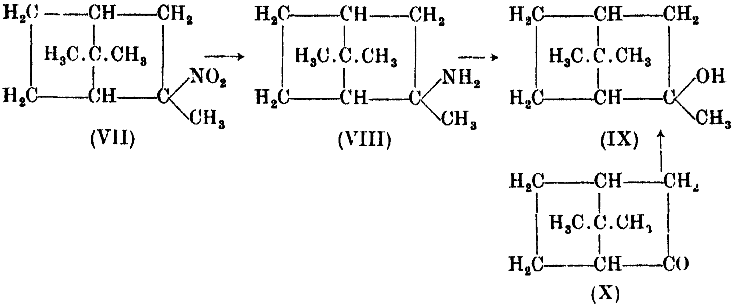
---

[*] *Ber.* 1912, **45**, 3205; Ipatiev and Pines, *J. Amer. C.S.* 1945, **67**, 1931.

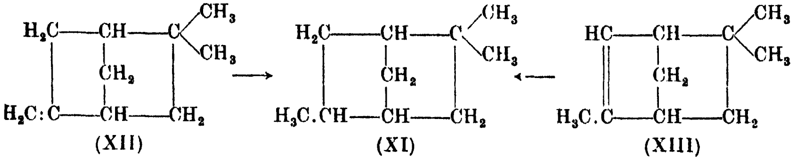
[†] *Annalen*, 1929, **476**, 63.

[‡] *Ibid.* 1934, **508**, 205.

[§] Toivonen, *J. pr. Chem.* 1941 [ii], **159**, 70.


(VII) (VIII) (IX) (X)

According to Nametkin, *iso*bornylol on dehydration under acid conditions gives a hydrocarbon, b.p. 153–155°/749 mm., $d_{4^\circ}^{20^\circ}$ 0·8628, $n_D^{20^\circ}$ 1·4695, values in fairly good agreement with those found for *dl*-α-fenchene; on reduction, however, it does not give *iso*bornylane, but a hydrocarbon, b.p. 160–161°/753 mm., $d_{4^\circ}^{20^\circ}$ 0·8541, $n_D^{20^\circ}$ 1·4567, termed *β-fenchane*, and formulated as (XI). Nametkin therefore concluded that the unsaturated hydrocarbon was a mixture of β-fenchene (XII) and γ-fenchene (XIII), and this is supported by the observation of Komppa and Beckmann[†] that, under acid conditions, α-fenchene is isomerised to such a mixture. Furthermore, the properties of β-fenchane, b.p. 158–160°, $d_{4^\circ}^{20^\circ}$ 0·8553, $n_D^{20^\circ}$ 1·4574, obtained by the catalytic hydrogenation of β-fenchene over a palladium catalyst[‡] are in good agreement with those of the saturated hydrocarbon described by Nametkin; on nitration it gives tert.*-nitro-β-fenchane*


(XII) (XI) (XIII)

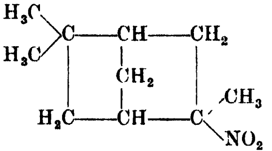
---

[*] *Annal. Acad. Sci. Fennicae,* 1916 [A], **10** [iii], 3.

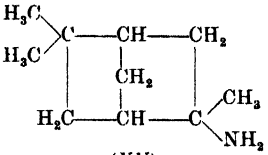
[†] *Annalen,* 1940, **543**, 111.

[‡] Komppa and Beckmann, *Annalen,* 1934, **508**, 205.

(XIV), b.p. 111°/10 mm., which is reduced by tin and hydrochloric acid to the *amino-β-fenchane* (XV) (*benzoyl* derivative, m.p. 156–157°).[*]

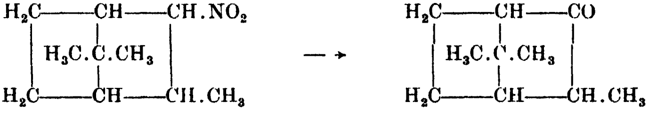


(XIV)



(XV)

The second *nitro*iso*bornylane* (XVI), b.p. 89–90°/1·2 mm., $d_{4°}^{20°}$ 1·0466, $n_D^{20°}$ 1·4805, to which reference was made above, contains a secondary nitro group, since on oxidation it yields a ketone, iso*bornylone* (XVII), b.p. 197·5–198°/762 mm., $d_{4°}^{20°}$ 0·9681, $n_D^{20°}$ 1·494 (*semicarbazone*, m.p. 174–175°), and *cis*-apocamphoric acid. Interest attaches to the preparation of this ketone, since it has the constitution at one time considered to be that of fenchone (compare p. 562).



(XVI) (XVII)

THE FENCHENES

Although Bouchardat and Tardy[†] have reported the isolation from the oil of *Eucalyptus globulus* of a terpene yielding on treatment with benzoic acid fenchyl alcohol, it is extremely doubtful if fenchene is actually present in this oil, since, as has been mentioned on p. 156, both α- and β-pinene give this alcohol on hydration.

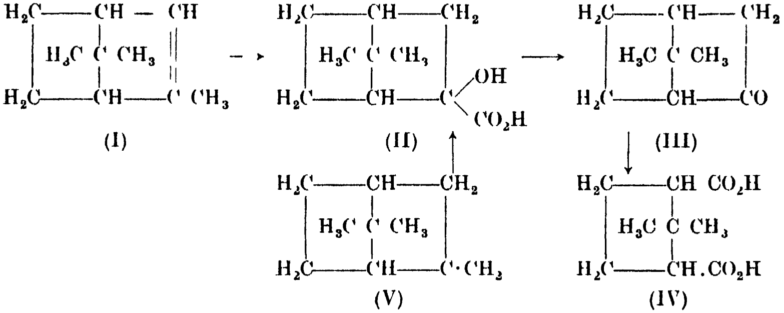
During his early experiments with the ketone, fenchone, Wallach[‡] reduced it to the corresponding alcohol, fenchyl alcohol, and prepared from this, by the action of phosphorus pentachloride, a chloride, which gave on removal of hydrogen chloride with aniline an optically inactive hydrocarbon, $C_{10}H_{16}$, b.p. 158–160°, to which the name fenchene was given. This hydrocarbon gave on oxidation with potassium permanganate an acid, $C_{10}H_{16}O_3$, which melted at 137–138°. The reactions of the hydrocarbon were discussed in a further series of communications[*] and the boiling-point was found to be somewhat lower, 154–156°. A more thorough investigation of its oxidation products showed the main product to be a hydroxy acid, $C_{10}H_{16}O_3$, m.p. 152–153°, which was evidently an α-hydroxy acid, since it gave with potassium permanganate in acid solution a ketone, *fenchocamphorone*, $C_9H_{14}O$. The constitution of the latter was established by its oxidation with nitric acid to *apocamphoric acid* (IV). Wallach concluded from these experiments that fenchene must be represented by (I), the hydroxy acid, m.p. 152–153°, being (II) and fenchocamphorone (III).

---

[*] Toivonen, Alfthan, Böök, Erich and Heino, *J. pr. Chem.* 1941 [ii], **159**, 70.

[†] *Compt. rend.* 1895, **120**, 1418.

[‡] *Annalen*, 1891, **263**, 129.



It is obvious that the reactions outlined above would be more simply explained if fenchene had formula (V), but at the time of these experiments it was considered improbable that hydrocarbons with an exocyclic ethylenic linkage were capable of existence and, as mentioned on p. 192, Baeyer regarded nopinic acid as an oxidation product of α-pinene. Later, Wallach[†] adopted formula (V) for fenchene.

In 1898 Gardner and Cockburn,[‡] who were also engaged in a study of the reactions of *d*-fenchone, prepared a fenchene, b.p. 152–154°, which, like Wallach's hydrocarbon, gave on oxidation with nitric acid apocamphoric acid, but differed from it in being optically active, $[\alpha]_D$ −6·46°.

A renewed study of the fenchyl chlorides by Wallach[§] showed that the optical rotatory powers of these differed considerably and depended upon the conditions used in their preparation. Thus *l*-fenchyl alcohol (from *d*-fenchone) could yield both dextro- and laevo-rotatory fenchyl chlorides. These in their turn gave rise to different fenchenes, which appeared to be structural isomerides, since on oxidation they gave rise to different fenchocamphorones. The possibility of the existence of a second fenchene was supported by the experiments of Bertram and Helle[*] who, by the hydration of a laevorotatory fenchene (from fenchyl chloride), prepared a new alcohol, *iso*fenchyl alcohol, which was also laevorotatory, but which gave on dehydration with zinc chloride in benzene solution a dextrorotatory fenchene, b.p. 155–156°, yielding on oxidation a hydroxy acid and a ketone differing from those described by Wallach. In the same year a third fenchene was obtained by Tschugaev[†] by the distillation of methyl fenchylxanthate.

---

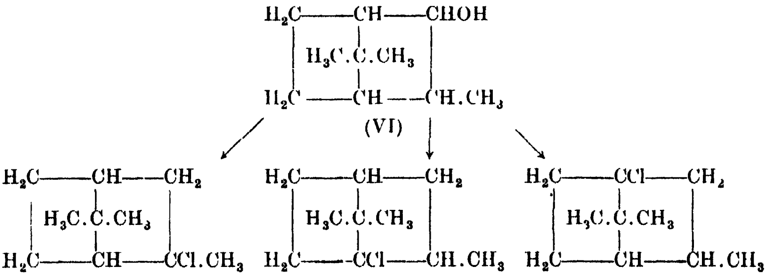
[*] *Annalen*, 1894, **284**, 331; 1898, **300**, 294, 319.

[†] *Ibid.* 1901, **315**, 273.

[‡] *J.C.S.* 1897, **71**, 1156; 1898, **73**, 275.

[§] *Annalen*, 1898, **302**, 371.

At this time Wallach held the view that the variation in the optical rotatory power of the different fenchyl alcohols was due to stereoisomerism and that no molecular rearrangement occurred during their formation. This opinion was not shared by Kondakov and Lutschinin,[‡] who considered that secondary alcohols on treatment with halogen acids (or phosphorus pentachloride) gave tertiary chlorides. They regarded fenchyl chloride as a mixture of tertiary chlorides for which, on the basis of Wallach's formula (VI) for fenchyl alcohol, formulae (VII), (VIII) and (IX) were possible. Elimination of hydrogen chloride might therefore be expected to yield a number of isomeric fenchenes.


(VI)
(VII) (VIII) (IX)

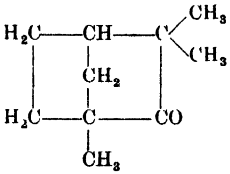
---

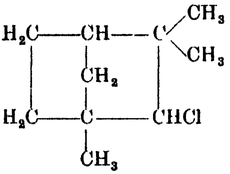
[*] *J. pr. Chem.* 1900 [ii], **61**, 293.

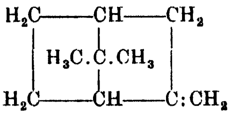
[†] *Chem.-Ztg.* 1900, **24**, 542.

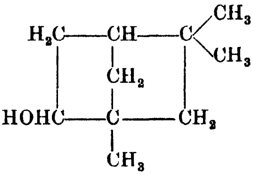
[‡] *J. pr. Chem.* 1899 [ii], **60**, 257; 1900 [ii], **62**, 1; 1902 [ii], **65**, 201.

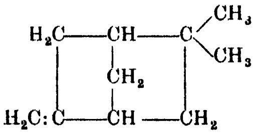
The position was radically changed by the replacement of Wallach's formula for fenchone by that of Semmler (X) (compare p. 563), since, even if it were assumed that fenchyl chloride had formula (XI), a molecular rearrangement must occur in the formation of Wallach's fenchene (V).


(X)


(XI)


(V)


(XII)


(XIII)

The difference in properties between Wallach's fenchene and that prepared by Bertram and Helle from *iso*fenchyl alcohol (XII) was also accounted for, the latter hydrocarbon being probably represented by (XIII), although, as Wallach and Virck* pointed out, this hydrocarbon was probably not homogeneous.

Later the chemistry of the fenchenes was very thoroughly investigated, especially by Komppa, Aschan, Qvist and Toivonen. These researches have shown that it is possible to prepare from fenchone six isomeric dicyclic hydrocarbons and a tricyclic hydrocarbon. Before proceeding to consider the chemistry of these it is desirable to discuss their nomenclature.

In order to distinguish between the various optically active fenchenes, Wallach† had introduced a somewhat cumbrous nomenclature, using a capital D- or L- to denote the relationship to *d*- or *l*-fenchones, a small *d*- or *l*- being used to denote the direction of their optical rotatory power. Thus the hydrocarbon represented by (V), when derived from *d*-fenchone, was laevorotatory and was known as D-*l*-fenchene, whilst Bertram and

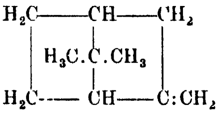
---

* *Annalen*, 1908, **362**, 193.

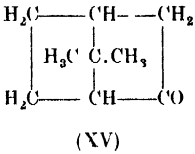
† *Ibid.* 1898, **302**, 374.

Helle's hydrocarbon (XIII) was D-*d*-fenchene. This nomenclature has now been replaced by the following, suggested by Komppa,* which will be used in the sequel.

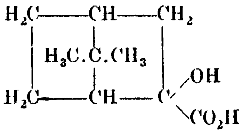
1. α-*Fenchene* (XIV) (Wallach's D-*l*-fenchene or L-*d*-fenchene), corresponding to α-*fenchocamphorone* (XV) and *hydroxy*-α-*fenchenic acid* (XVI).



(XIV)

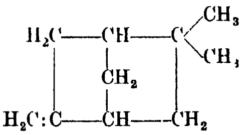


(XV)

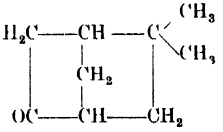


(XVI)

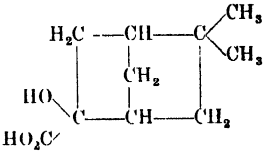
II. β-*Fenchene* (XVII) (Wallach's D-*d*-fenchene or L-*l*-fenchene), corresponding to β-*fenchocamphorone* (XVIII) and *hydroxy*-β-*fenchenic acid* (XIX).



(XVII)

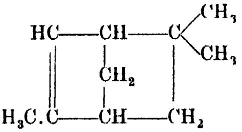


(XVIII)



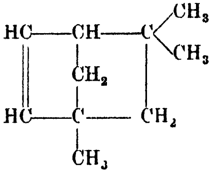
(XIX)

III. γ-*Fenchene* (XX).



(XX)

IV. δ-*Fenchene* (XXI).

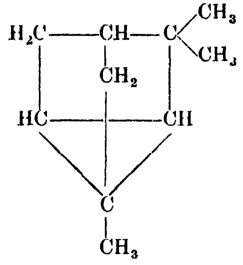


(XXI)

---

* Compare Komppa and Roschier, *Annalen*, 1929, **470**, 129.

V. cyclo*Fenchene* [Aschan's β-pinolene (XXII)].



(XXII)

More recently, ε-fenchene and ζ-fenchene have been described. Reference to them is made below.

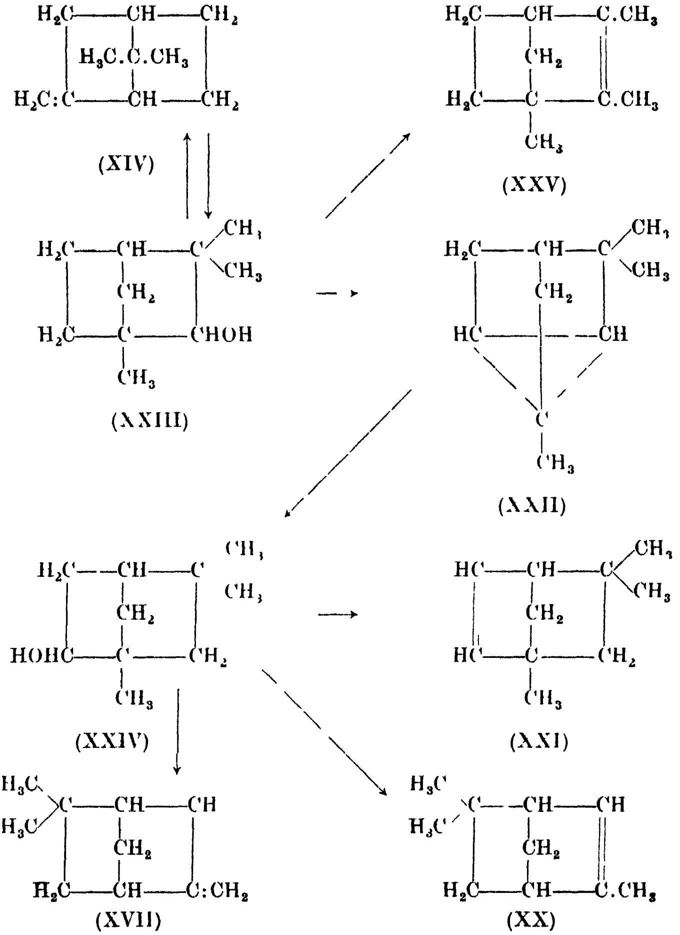
There are three general methods available for the preparation of the fenchenes: (i) direct dehydration of fenchyl and *iso*fenchyl alcohols, (ii) distillation of methyl fenchyl- and *iso*fenchyl-xanthates, and (iii) elimination of hydrogen chloride from fenchyl and *iso*fenchyl chlorides. Inspection of the formulae of the two alcohols (XXIII) and (XXIV) shows that, assuming no molecular rearrangement to occur, fenchyl alcohol should yield *cyclo*fenchene (XXII), whilst *iso*fenchyl alcohol can yield a mixture of this hydrocarbon and δ-fenchene (XXI); the same hydrocarbons should result also from the xanthates and the chlorides, assuming the latter to be homogeneous.

Investigation has, however, shown that in no case does the reaction proceed smoothly and unaccompanied by molecular rearrangement, a mixture of hydrocarbons being obtained in which one or another may predominate. The nature of the products obtained by the dehydration of fenchyl alcohol (XXIII) under various conditions has been further studied by Toivonen* and by Komppa and Nyman.† With non-acidic catalysts, the main product is α-fenchene (XIV), but in the presence of acids β-fenchene (XVII), γ-fenchene (XX), δ-fenchene (XXI), *cyclo*fenchene (XXII), and 1-*methylsantene* (*ε-fenchene*) (XXV) are formed.‡ The conversion of fenchyl alcohol into α-fenchene involves a normal Wagner rearrangement, whilst methylsantene is the result of a pinacolic change of the Nametkin type. The β-, γ-, and δ-fenchenes, however, cannot be directly formed by either of these types of isomerisation, and a possible explanation is that

---

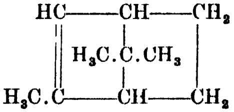
* *Inter al., Suomen Kem.* 1936, A **9**, 72; B **9**, 15. † *Annalen*, 1938, **535**, 252.

‡ Apparently the 1-methylsantene is derived only from the α-form of fenchyl alcohol, since it is not obtained when the pure β-stereoisomer is dehydrated under the same conditions.



they are derived from *iso*fenchyl alcohol (XXIV), which can arise by hydration of *cyclo*fenchene. Dehydration of *iso*fenchyl alcohol without rearrangement would yield δ-fenchene, whilst β- and γ-fenchenes would be formed by a Wagner rearrangement. The formation of the latter hydrocarbons from α-fenchene, under acid conditions[*] may also occur by the same route. *cyclo*Fenchene thus occupies a key position in these interconversions, and it is important to note that, unlike tricyclene, the properties of which prove that it cannot be an intermediate in the borneol-camphene change, the properties of *cyclo*fenchene are not incompatible with the above hypothesis (see also p. 551).

On theoretical grounds, a further isomeric fenchene (XXVI) should be capable of existence, bearing the same relationship to α-fenchene (XIV) as γ-fenchene (XX) does to β-fenchene (XVII). Hückel and Kindler[†] have recently succeeded in preparing this substance, named ζ-fenchene (the term ε-fenchene having already been applied to 1-methylsantene), by treatment of β-fenchyl *p*-toluenesulphonate with sodium *iso*propoxide.

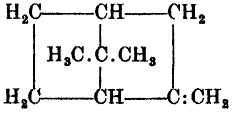


(XXVI)

In view of the readiness with which these rearrangements occur, it is improbable that any of the fenchenes, with the exception of *cyclo*fenchene, have been obtained in a state of purity.

The account of the earlier work on the chemistry of the fenchenes given below, unless other references are quoted, has been summarised from the investigations of Wallach,[‡] Aschan,[§] Komppa and Hintikka,[‖] Komppa and Roschier,[¶] Qvist[**] and Ruzicka and Liebl.[††]

α-*FENCHENE*



α-Fenchene, of which both the dextro- and laevo-rotatory forms are known, was probably the hydrocarbon originally prepared by

---

[*] Komppa and Nyman, *Annalen*, 1940, **543**, 111.

[†] *Chem. Ber.* 1947, **80**, 197.

[‡] *Annalen*, 1908, **362**, 186.

[§] *Ber.* 1907, **40**, 2750; *Annalen*, 1912, **387**, 1.

[‖] *Ber.* 1914, **47**, 936.

[¶] *Annalen*, 1929, **470**, 129.

[**] *Ibid.* 1918, **417**, 278.

[††] *Helv. Chim. Acta*, 1923, **6**, 267.

Wallach* by the action of aniline on fenchyl chloride. As has been shown by Qvist, the yield of hydrocarbon when hydrogen chloride is eliminated from fenchyl chloride, either by the action of aniline or *o*-toluidine, is very poor. Better results are obtained by the dehydration of fenchyl alcohol with phthalic anhydride, or by the distillation of methyl-α-fenchocamphorol (see p. 541).[1] α-Fenchene can also be conveniently prepared in quantity either by the distillation of methyl α-fenchylxanthate or by the action of nitrous acid on fenchylamine.

When prepared from *l*-fenchylamine, *l*-α-fenchene has b.p. 156–157°, $d^{19°}$ 0·869, n_D^{19} 1·4724, $[\alpha]_D$ −32·12°, whilst for the dextrorotatory hydrocarbon from *d*-fenchylamine, $[\alpha]_D$ +29° has been observed. The hydrocarbon prepared from either fenchyl chloride or fenchyl alcohol has as a rule a lower rotatory power. It can readily be identified by the preparation of the crystalline *dibromide*, the *d*- and *l*-forms of which melt at 87–88°, $[\alpha]_D$ +42·83° (in ethyl acetate), whilst the *dl*- has m.p. 62°.

The constitution of α-fenchene has been conclusively proved by an investigation of its degradation products and also by a complete synthesis of these and of α-fenchene itself by Komppa and his collaborators. As has already been mentioned Wallach, in his early experiments, investigated the oxidation of *l*-α-fenchene (I) and showed that with potassium permanganate it gave a hydroxy acid, 1-*hydroxy-α-fenchenic acid* (II) (*d*- and *l*-forms, m.p. 153–154°), from which by the action of lead peroxide in the presence of sulphuric acid (or acid potassium permanganate) 1-*α-fenchocamphorone* (III), *d*- and *l*-forms, m.p. 109–110°, b.p. 202°, *semicarbazone*, m.p. 220–221°, was obtained. This ketone gave on oxidation with nitric acid cis-*apocamphoric acid* (IV).

This formula for α-fenchene was confirmed by Komppa and Roschier‡ who showed that on ozonolysis α-fenchocamphorone (III) was obtained, the ketone being, however, accompanied by a saturated acid, $C_{10}H_{16}O_2$ (V), the constitution of which, and the mechanism of its formation, will be discussed below.

In 1901, Komppa§ described a synthesis of *cis*- and *trans*-apocamphoric acids (IV), and this synthesis was subsequently extended to a synthesis of *dl*-α-fenchocamphorone (III)* and finally to *dl*-α-fenchene (I).† These syntheses are outlined in the scheme set out below and do not require comment.

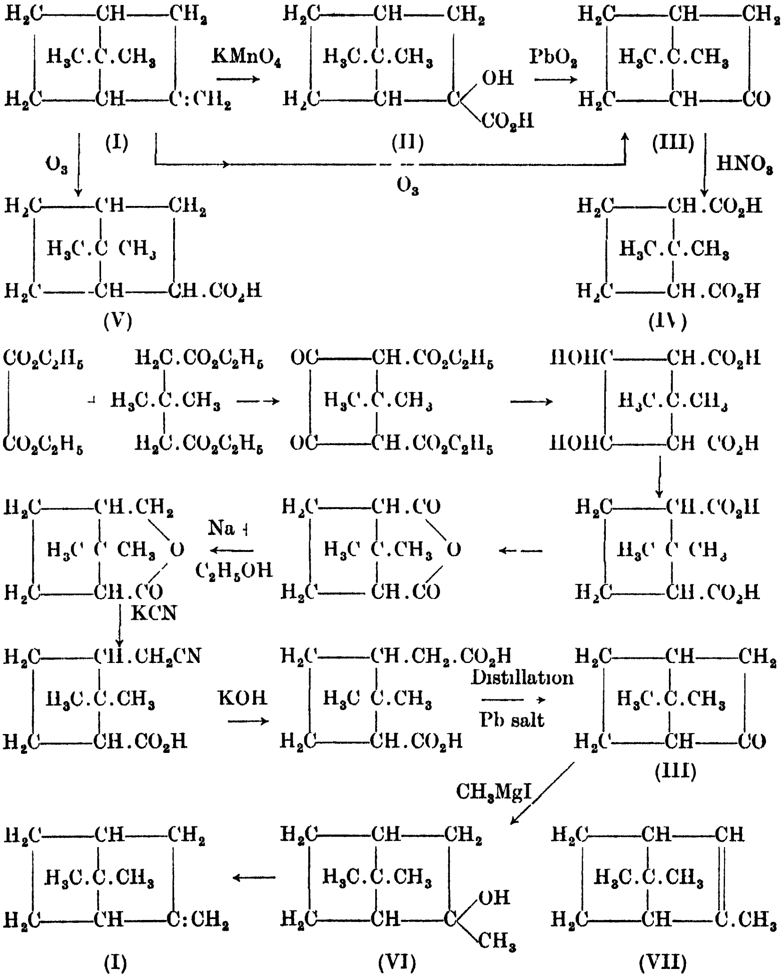
---

* *Annalen*, 1891, **263**, 129.

† Komppa and Nyman, *Annalen*, 1938, **535**, 252; 1940, **543**, 111.

‡ *Annal. Acad. Sci. Fennicae*, 1917 [A], **10** [xviii], 1.

§ *Ber.* 1901, **34**, 2472; *Annalen*, 1909, **368**, 126.



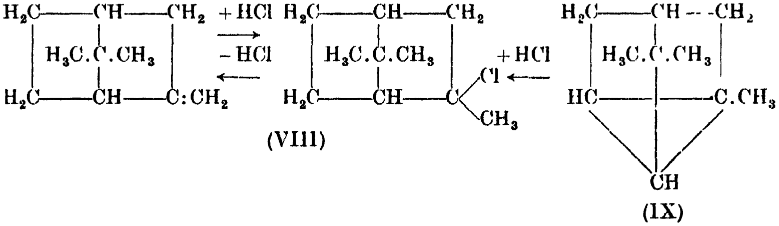
The alcohol, dl-*methyl-α-fenchocamphorol* (*α-fenchene hydrate*) (VI), m.p. 46–47°, b.p. 87°/14 mm. (*phenylurethane*, m.p. 117–

---

* *Ber.* 1911, **44**, 1536.

† Komppa and Roschier, *Annal. Acad. Sci. Fennicae*, 1916 [A], **10** [iii], 3; Komppa and Beckmann, *Annalen*, 1934, **508**, 205.

118°), on distillation at the ordinary pressure lost water, giving *dl*-α-fenchene (I), b.p. 154–156°, $d_{4°}^{20°}$ 0·8660, $n_D^{20°}$ 1·4704, the constants of the synthetic hydrocarbon agreeing well with those of the hydrocarbon prepared from *l*-fenchylamine (p. 539). The elimination of water from the alcohol can theoretically result also in the formation of a hydrocarbon having the structure (VII),[*] which according to Aschan[†] belonged to *iso*pinene, which he prepared from *cyclo*fenchene hydrochloride. Komppa and Roschier found, however, that *dl*-α-fenchene could not have formula (VII) since it gave on ozonolysis *dl*-α-fenchocamphorone and *dl*-α-fenchenylanic acid (V). They also showed Aschan's *iso*pinene to be identical with *dl*-α-fenchene, both hydrocarbons giving the same products on oxidation, whilst on treatment with hydrogen chloride they both yield *dl-α-fenchene hydrochloride* (VIII), m.p. 35–37°, b.p. 81°/12 mm., which on treatment with dilute alkali gives *dl*-methyl-α-fenchocamphorol (VI).[‡] It would appear to be not improbable that *cyclo*fenchene hydrochloride, m.p. 26–29°, derived from *cyclo*fenchene (IX), is stereoisomeric with this, though it behaves differently on treatment with alkali (see p. 551).[§] It is of interest to note that dehydration of methyl-α-fenchocamphorol in the presence of acid catalysts gives mainly β- and γ-fenchenes, since α-fenchene is converted into these isomers under such conditions.[||] (Compare p. 545.)



(VIII)

(IX)

On hydrogenation over a nickel or palladium catalyst, α-fenchene gives iso*bornylane* (*α-fenchane*).

---

[*] This formula is now assigned to ζ-fenchene (see p. 549).

[†] *Öfvers. Finska Vet. Soc.* 1908–1909, **51** A, no. 9, 10.

[‡] Komppa and Beckmann, *Annalen*, 1934, **508**, 205.

[§] The hydrocarbon, *α-pinolene*, obtained by Aschan by the action of alkali on the liquid hydrochlorides prepared by the action of hydrogen chloride on pinene is not improbably a mixture of fenchenes, since it gave with hydrogen chloride α-fenchene hydrochloride.

[||] Komppa and Nyman, *Annalen*, 1940, **543**, 111.

It was mentioned above that, on ozonolysis, α-fenchene gave not only α-fenchocamphorone, but also a saturated acid, α-*fenchenylanic acid*, *d*-form, m.p. 71–72°, *dl*-, m.p. 104–105°, to which formula (V) has been assigned. This has been supported by a synthesis from α-fenchocamphorone (III), which on reduction with sodium and alcohol yields *α-fenchocamphorol* (*apoborneol*) (X), m.p. 122–124°, converted by phosphorus pentachloride into *apobornyl chloride* (XI), m.p. 24–25°.[*] On treatment with magnesium and carbon dioxide this gives α-fenchenylanic acid, the structure of which is thus confirmed, provided that no rearrangement has occurred.[†] With aniline, apobornyl chloride gives a mixture of *apocyclene* (XII), and *apo*iso*fenchene* (XIII), whilst with potassium amyloxide it yields *apobornylene* (XIV)[‡] (compare p. 331).

Although Komppa and Roschier have suggested that α-fenchenylanic acid is formed by a somewhat unusual rearrangement of the ozonide, this is no longer likely, in view of the modified views now held concerning the structures of ozonides. If the acid is truly represented by (V) it is possible, however, to postulate a scheme, shown on p. 543, by which it could be formed from the oxide (XV) by rearrangement to the aldehyde (XVI). Indirect support for the structure of fenchenylanic acid has been provided by Treibs and Schmidt[§] who have shown that the acid is formed, together with *fenchenylanaldehyde* (XVI) and α-fenchocamphorone, by the oxidation of α-fenchene with chromic acid, the reaction thus proceeding in a manner similar to that encountered in the case of camphene (p. 297).

On treatment with bromine in acetic acid solution, α-fenchene gives a *dibromide*, *d*- and *l*-forms, m.p. 87–88°, $[\alpha]_D$ ± 43° (in ethyl acetate); *dl*-form, m.p. 62°.[‖] The optically active dibromide has a sign of rotation opposite to that of the α-fenchene from which it is derived. Reduction of the *d*-dibromide with zinc dust in alkaline solution gives a mixture of *l*-α-fenchene and fenchane, a partial Wagner rearrangement being involved. Rearrangement also occurs when α-fenchene is hydrated with acetic-sulphuric acid, *iso*fenchyl alcohol being formed.

---

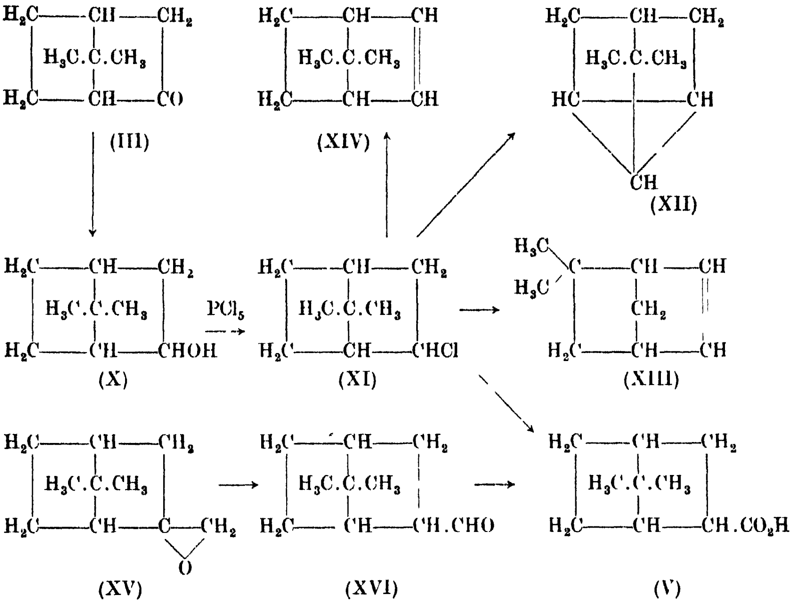
[*] This is probably stereoisomeric with *apocyclene hydrochloride*, m.p. 44–46°, which on hydrolysis with dilute alkali gives α-iso*fenchocamphorol*, m.p. 132–133°, a stereoisomer of α-fenchocamphorol (Komppa and Nyman, *Ber.* 1936, **69**, 1813).

[†] Compare the analogous reaction with bornyl chloride, p. 343.

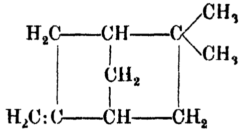
[‡] Komppa and Hasselström, *Annalen*, 1932, **497**, 116.

[§] *Ber.* 1928, **61**, 459.

[‖] Wallach and Virck, *Annalen*, 1908, **362**, 182; compare Kondakov, *J. pr. Chem.* 1909 [ii], **79**, 277.



β-FENCHENE



d-β-Fenchene (IV) was first prepared by Bertram and Helle[*] by the dehydration of l-iso*fenchyl alcohol* (I), and shortly afterwards by Wallach and Neumann[†] by the action of aniline on a fenchyl chloride prepared by allowing phosphorus pentachloride to act upon *l*-α-fenchyl alcohol in light petroleum solution without cooling. It is probably best obtained pure either by the dehydration of l-α-*fenchyl alcohol* (II) with potassium hydrogen sulphate

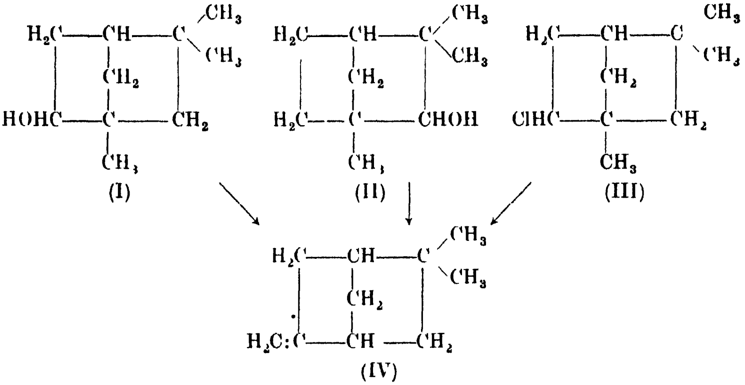
---

[*] *J. pr. Chem.* 1900 [ii], **61**, 353.

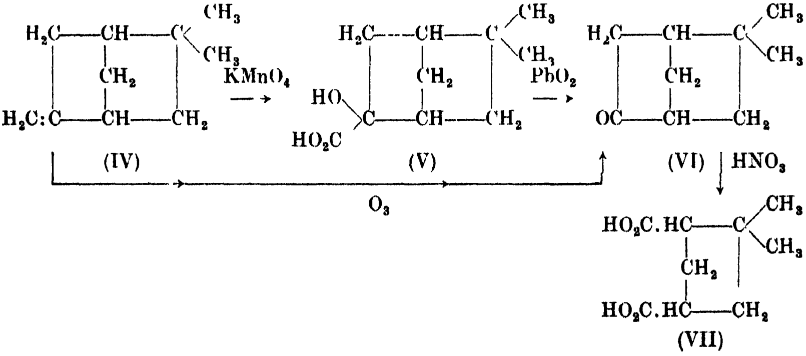
[†] *Annalen*, 1901, **315**, 281.

(Komppa and Roschier) or by the elimination of hydrogen chloride from l-iso*fenchyl chloride* (III) with *o*-toluidine (Qvist).

When prepared by the latter method *d*-β-fenchene has b.p. 150–153°, d_4^{20} 0·8591, $n_D^{18\cdot 6}$ 1·4645, $[\alpha]_D$ + 62·91°. It can be characterised by the preparation of the crystalline *dibromide*, m.p. 81–82°, or the *nitrosochloride*, m.p. 120°.



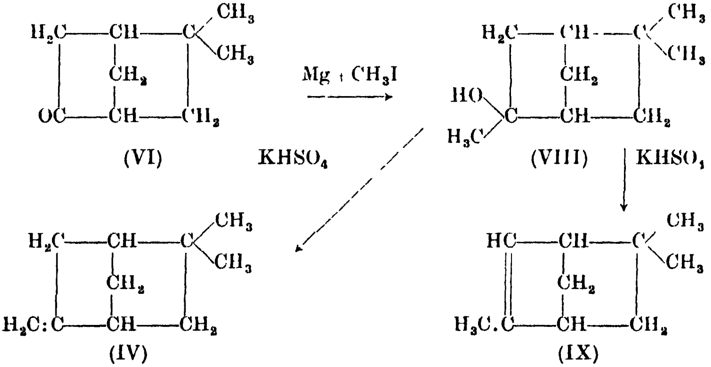
On oxidation with potassium permanganate, *d*-β-fenchene behaves in an analogous manner to α-fenchene, yielding a hydroxy acid, d-*hydroxy-β-fenchenic acid* (V), m.p. 137–138° (*dl*-, m.p. 125–126°), from which, by the action of lead peroxide in the presence of sulphuric acid, d-*β-fenchocamphorone* (VI), m.p. 62–63° (*dl*-, m.p. 64–66°), can be prepared. This ketone on oxidation with hot potassium permanganate or nitric acid yields *apofenchocamphoric acid* (VII), *cis*-, m.p. 144·5–145°, *trans*-,



m.p. 147–148°, whilst on reduction with sodium and alcohol it gives *β-fenchocamphorol*, m.p. 64–65°, b.p. 198–199° (*hydrogen phthalate*, m.p. 126–127°; *phenylurethane*, m.p. 96–97°), and its stereoisomer, *β-isofenchocamphorol*, m.p. 60–61° (*hydrogen phthalate*, m.p. 130–131°).[*]

The structure assigned to β-fenchene has been confirmed by its oxidation with ozone to β-fenchocamphorone.

A partial synthesis of β-fenchene was carried out by Komppa and Roschier[†] on the lines of their synthesis of α-fenchene (compare p. 540). By the action of methyl magnesium iodide on β-fenchocamphorone they prepared *methyl-β-fenchocamphorol* (VIII),[‡] m.p. 86–87°, which on dehydration with potassium hydrogen sulphate gave a mixture of β-fenchene (IV) and γ-fenchene (IX).



The synthesis of β-fenchocamphorone has been attended with considerable difficulty.[§] Short[‖] prepared apofenchocamphoric acid synthetically by the condensation of ethyl disodiopropane-αα′γγ′-tetracarboxylate (X) with *iso*butylene dibromide (XI), whilst Bardhan, Banerji and Bose[¶] described a synthesis of *homoapofenchocamphoric acid* (XII), m.p. 246°.

---

[*] Komppa and Beckmann, *Annalen*, 1939, **537**, 140.

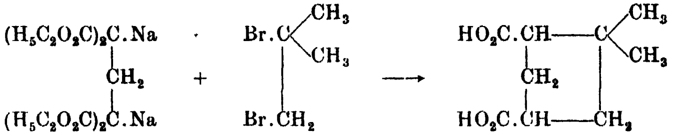
[†] *Annal. Acad. Sci. Fennicae*, 1917 (A), **15** [x], 1.

[‡] A stereoisomeric form of this alcohol, termed *β-fenchene hydrate*, m.p. 67°, has been obtained from *iso*fenchyl alcohol (see p. 559).

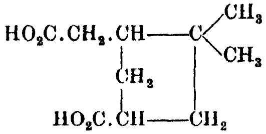
[§] Compare Komppa and Komppa, *Ber.* 1936, **69**, 2606.

[‖] *J.C.S.* 1927, p. 961. A more convenient synthesis has recently been described by Mukherji (*Science and Culture*, 1948, **13**, 388).

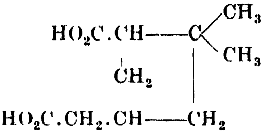
[¶] *J.C.S.* 1935, p. 1127.



(X) (XI) (VII)

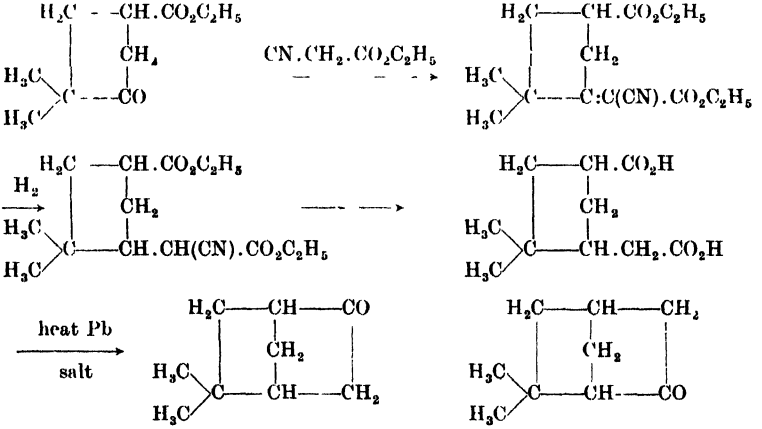


(XII)



(XIIa)

At the time, the latter compound was obtained in a quantity insufficient to enable a study to be made of its cyclisation into β-fenchocamphorone, but more recently,* as a result of an improved synthesis, shown below, success has been achieved, the ketone being formed by pyrolysis of the lead salt of the synthetic acid:



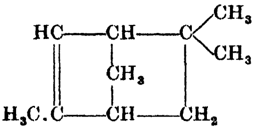
(VI) (VIa)

With hydrogen chloride, β-fenchene gives an oily *hydrochloride*, which is reconverted into the hydrocarbon on treatment with an organic base. On hydration, β-fenchene gives *iso*fenchyl alcohol.

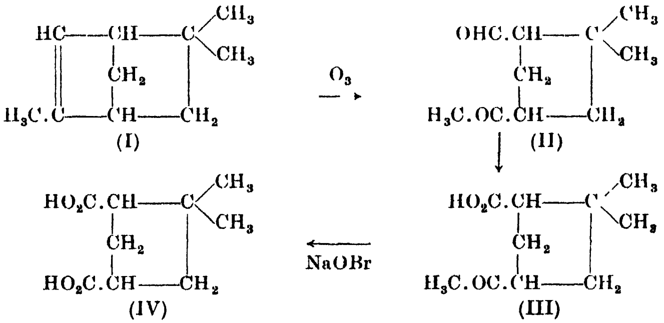
---

* Mukherji and Bardhan, *J.C.S.* 1949, p. 195. Mukherji (*Science and Culture*, 1948, 13, 388) has described the synthesis of the isomeric homoapofenchocamphoric acid (XIIa). When the lead salt of this acid is heated, it yields β-iso-*camphenilone* (VIa).

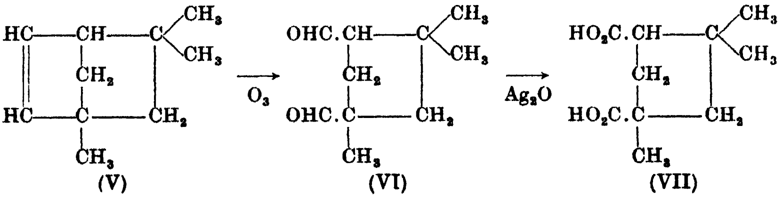
γ-*FENCHENE*



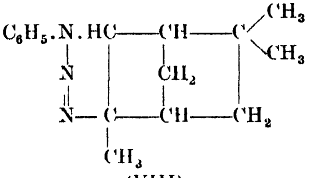
γ-Fenchene has not been obtained pure, but it forms the main constituent of the hydrocarbon fraction, b.p. 145–147°, $d_{4°}^{20°}$ 0·8547, $n_D^{20°}$ 1·4607, which is obtained when α-fenchyl alcohol is dehydrated with potassium hydrogen sulphate. This was shown by the fact that, on ozonolysis, the main products were (i) an *aldehyde*, $C_{10}H_{16}O_2$ (II), *disemicarbazone*, m.p. 219°, and (ii) a *ketonic acid*, $C_{10}H_{16}O_3$ (III), *semicarbazone*, m.p. 220–221°. The constitution of the latter was established by its oxidation with sodium hypobromite to trans-*apofenchocamphoric acid* (IV).



Whilst the isolation of these products leaves no doubt as to the constitution of the hydrocarbon which was oxidised, it was not homogeneous, since, when the crude aldehyde (II) was oxidised with silver oxide, it gave, in addition to the ketonic acid (III), cis-iso*fenchocamphoric acid* (VII), which could only have resulted from the degradation of δ-*fenchene* (V), the primary oxidation product of which would be the *dialdehyde* (VI).

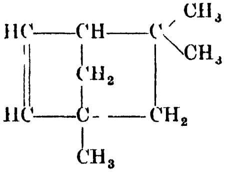


γ-Fenchene gives a crystalline *adduct*, probably (VIII), m.p. 177°, with phenyl azide;[*] it also forms a *nitrosate*, m.p. 146–147° (decomp.), and a *nitrosochloride*, m.p. 150° (decomp.).[†] On hydration, it gives *iso*fenchyl alcohol.



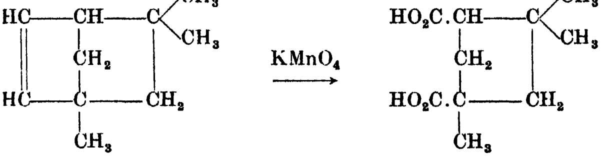
(VIII)

δ-*FENCHENE*



δ-Fenchene, known also as *fenchylene*,[‡] iso*fenchylene* (Qvist), or iso*fenchene* (Komppa), has not been prepared pure and free from *cyclo*fenchene. It is present in the lowest boiling hydrocarbon fraction which is obtained (i) when α-fenchyl alcohol is dehydrated with potassium hydrogen sulphate, or (ii) by the distillation of methyl *iso*fenchylxanthate. According to Nametkin, the hydrocarbon derived from the *l*-xanthate boils at 139–140°/762 mm., $d_{4°}^{20°}$ 0·8381, $n_D^{20°}$ 1·4494, $[\alpha]_D$ −68·76° (in alcohol). It can be characterised by the preparation of a *nitrosochloride*, m.p. 142°, and a *nitrosate*, m.p. 163°.

The constitution of the hydrocarbon (I) follows from the fact that on oxidation with potassium permanganate it yields cis-iso*fenchocamphoric acid* (II).



(I) (II)

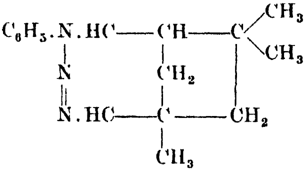
---

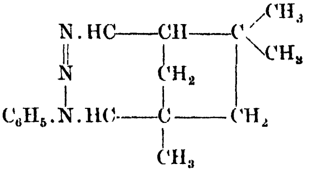
[*] Alder and Stein, *Annalen*, 1933, **501**, 1.

[†] Komppa and Beckmann, *Ibid.* 1933, **503**, 130.

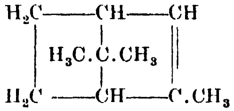
[‡] Nametkin, *J. pr. Chem.* 1923 [ii], **106**, 26.

With phenyl azide, δ-fenchene gives two *adducts*, m.p.'s 122° and 128–129°, respectively, which are probably represented by the structural isomers (III) and (IV).*

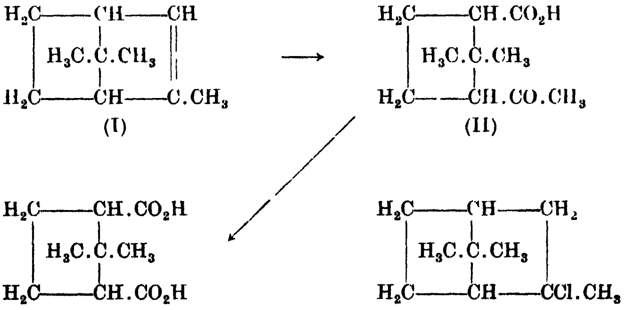

(III)


(IV)

ζ-FENCHENE



ζ-Fenchene (I) has been prepared by Hückel and Kindler† by heating β-fenchyl *p*-toluenesulphonate with sodium *iso*propoxide at 140°. The hydrocarbon was purified by fractional distillation, and then showed b.p. 146·2–146·8°/752 mm., $d_4^{20°}$ 0·8626, $n_D^{20°}$ 1·4685, $[\alpha]_D^{20°}$ −24·1°. Its Raman spectrum was also recorded. The constitution was proved by oxidation with potassium permanganate, when it gave cis-*apocamphoric acid* (III), via the *keto-acid* (II) (*semicarbazone*, m.p. 158–161°). The isolation of ζ-fenchene is of interest, since its structure was at one time allocated to the so-called "*iso*pinene" prepared by Aschan from *cyclo*fenchene hydrochloride (see p. 541).


(I) (II) (III) (IV)

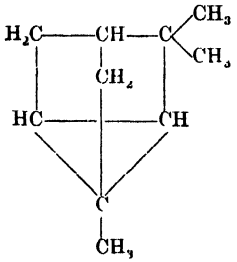
---

* Alder and Stein, *Annalen*, 1933, **501**, 1.

† *Chem. Ber.* 1947, **80**, 197.

No crystalline derivatives of the hydrocarbon have been described, the *hydrochloride* ($[\alpha]_D$ −41°), *nitrosochloride*, and *dibromide* having been obtained only as oils. The hydrochloride would be expected to have the constitution (IV), identical with one of the stereoisomeric forms of α-fenchene hydrochloride (p. 541), but this does not appear to be the case. Furthermore, ζ-fenchene hydrochloride, on treatment with bases, regenerates the same hydrocarbon and gives no α-fenchene. Further investigations on the structure of this derivative would be of interest.

CYCLO*FENCHENE*



*cyclo*Fenchene (β-pinolene) was first separated by Aschan in 1911 from the mixture of hydrocarbons which is obtained when the liquid hydrochlorides resulting from the action of hydrogen chloride on pinene are treated with alkali. It has since been shown to be present also in the lowest boiling fractions of the mixture of fenchenes prepared by any of the general methods given on p. 531. The simplest method for its preparation consists, however, in treating *d*-fenchonehydrazone with mercuric oxide in the presence of alkali* (compare p. 573). *cyclo*Fenchene can readily be obtained pure, since it is only very slowly attacked by potassium permanganate, and it can thus be freed from unsaturated hydrocarbons by shaking with this reagent at 60–80° for some hours.

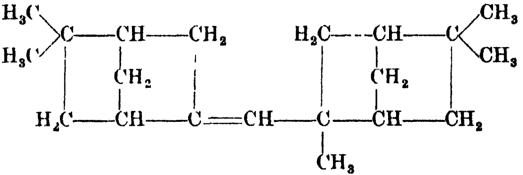
When prepared from *l*-fenchyl alcohol, the hydrocarbon is slightly laevorotatory ($[\alpha]_D$ −1·77°); for the carefully purified terpene Östling[*] gave the following constants: b.p. 143–143·5°/748 mm., $d_{4°}^{16.4°}$ 0·8624, $n_D^{16.2°}$ 1·4537, and values in close accord with these have been obtained by other investigators.

---

* G.P. 353933.

By the distillation of *cyclo*fenchene over platinum black in a current of hydrogen at 155–166°, Zelinski and Lewina[†] obtained *iso*bornylane (p. 529), whilst, when passed over the same catalyst in a current of carbon dioxide at 300°, ring fission occurs with the formation of a mixture of α- and β-fenchenes. A mixture of β- and γ-fenchenes is also obtained by treatment of *cyclo*fenchene with potassium bisulphate,[‡] whilst Ipatiev and Pines[§] have shown that it is converted into a mixture of bicyclic olefinic hydrocarbons (presumably fenchenes) when heated under pressure with aqueous magnesium chloride.

When *d-cyclo*fenchene ($[\alpha]_D$ + 1·0°) is treated with activated earth it forms *d-β-difenchene* (I), m.p. 83°, b.p. 171°/10 mm., $[\alpha]_D^{20°}$ + 67° in chloroform; similarly, *l-cyclo*fenchene gives *l-β-difenchene*, m.p. 83°, $[\alpha]_D^{22°}$ − 66° in chloroform. The *dl*-diterpene, prepared by admixture of the *d*- and *l*-forms, crystallises in prisms, m.p. 57°.[||] For an account of the reactions of these compounds, and the proof of structure, the original paper should be consulted.



(I)

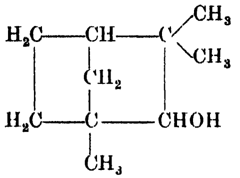
On treatment with bromine, *cyclo*fenchene yields *α-fenchene dibromide*, m.p. 86–87°, whilst with hydrogen chloride it gives a somewhat unstable *hydrochloride*, m.p. 26–29° (compare p. 541). On treatment with dilute alkali, the hydrochloride gives *β-fenchene hydrate* (p. 559). By the hydration of *cyclo*fenchene, *iso*fenchyl alcohol is obtained.

---

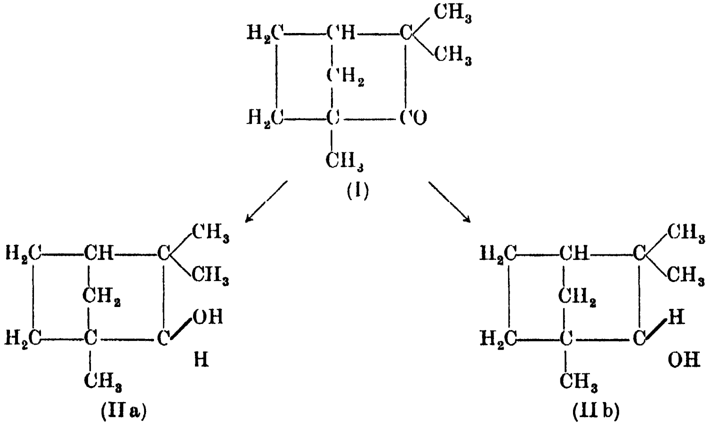
[*] *J.C.S.* 1912, **101**, 472.
[†] *Annalen*, 1929, **476**, 63.
[‡] Komppa and Nyman, *Annalen*, 1938, **535**, 252.
[§] *J. Amer. C.S.* 1945, **67**, 1931.
[||] Toivonen, Alfthan, Book, Erich and Heino, *J. pr. Chem.* 1941 [ii], **159**, 70.

B. ALCOHOLS

FENCHYL ALCOHOL



The occurrence in nature of fenchyl alcohol was first reported by Schimmel and Co.,[*] who isolated it from an oil obtained from old roots of *Pinus palustris*; this observation was subsequently confirmed by Zeitschel and Todenhöfer.[†] The dextro- and laevorotatory forms were prepared by Wallach[‡] by the reduction of *d*- and *l*-fenchones (I) with sodium and alcohol,[§] when the dextrorotatory ketone yields a laevorotatory alcohol, change of sign occurring.



It was recognised that fenchone, like camphor, should on reduction give two stereoisomeric alcohols (IIa) and (IIb) corresponding to borneol and *iso*borneol, and it was actually observed that the alcohol obtained by the reduction of fenchone was not homogeneous, since Bertram and Helle* found it convenient to purify it through its crystalline hydrogen phthalate. The separation of the two alcohols, l-α-*fenchyl alcohol* and l-β-*fenchyl alcohol*,† prepared by the reduction of *d*-fenchone, was first effected by Kenyon and Priston.‡ *l*-α-Fenchyl alcohol was readily obtained pure by the hydrolysis of its sparingly soluble *hydrogen phthalate*; the isomeric *l*-β-fenchyl alcohol, the hydrogen phthalate of which was readily soluble, was purified by crystallisation of its p-*nitrobenzoate*. According to Schmidt and Schulz§ the hydrogenation of fenchone over a nickel catalyst gives mainly the β-alcohol, whilst the α-isomer is the principal product when the reduction is carried out with sodium and alcohol. These authors have also described the dextro- and inactive modifications of both stereoisomers, whilst Huckel, Kindler and Wolowski‖ have prepared several new derivatives. The constants of the alcohols are given in the table below, and it is interesting to note that, whereas *d*-camphor gives on reduction *d*-borneol and *l*-*iso*borneol, both alcohols derived from *d*-fenchone are laevorotatory.

---

[*] *Schimmel's Report*, 1910, April.

J. pr. Chem. 1932 [ii], **133**, 374; compare Komppa and Beckmann, *Ber.* 1935, **68**, 10.

[‡] *Annalen*, 1891, **263**, 143; 1893, **272**, 104.

[§] Compare Gardner and Cockburn, *J.C.S.* 1898, **73**, 276.

The Stereoisomeric Fenchyl Alcohols

	M.p.	B.p.	$d_4^{20°}$	$[\alpha]_D^{20°}$ in EtOH	M.p.'s of derivatives Hydrogen phthalate	 *p*-Nitrobenzoate	 Phenylurethane
d-α-	47°	201	—	+11·5°	145°	—	81°
l-α-	48°	94°/20 mm	0·9641	−11·0°	146	108	82°
dl-α-	38°	200	—	± 0°	169°	—	104°
d-β-	—	—	—	+21·8°	151°	—	89°
l-β-	5°	201°	0·9630	−24·0°	154°	82	89°
dl-β-	6°	201°	—	± 0°	153°	—	90°

The constitution of the fenchyl alcohols is proved by their conversion on oxidation with chromic acid into fenchone, Kenyon and Priston observing that the *d*-fenchone obtained by the oxidation of both *l*-α- and *l*-β-fenchyl alcohols had the same rotatory power as the *d*-fenchone from which they were prepared. It appears probable that α-fenchyl alcohol corresponds in configuration to borneol.[*] In addition to the methods mentioned above, the reduction of fenchone to fenchyl alcohol has also been found to occur when the ketone is treated with ethyl magnesium iodide[†] or propyl magnesium iodide.[‡] *d*-α-Fenchyl alcohol has also been obtained by the hydration of laevorotatory oil of turpentine. The formation of this alcohol from pinene was first observed by Bouchardat and Lafont[§] to occur when the hydration was effected with concentrated sulphuric acid, but later the same investigators showed that a mixture of acetic and sulphuric acids could also be used.[‖] As is mentioned elsewhere, this reaction involves a Wagner rearrangement.

---

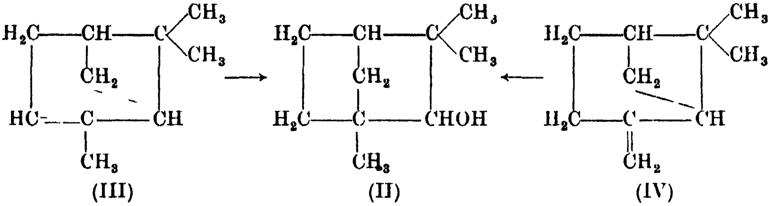
* *J. pr. Chem.* 1900 [ii], **61**, 294.

† The nomenclature is unfortunate; α- and β-fenchyl alcohols are thus *stereoisomerides*, whilst *iso*fenchyl alcohol (p. 557) is a *structural* isomeride.

‡ *J.C.S.* 1925, **125**, 1472.

§ *Schimmel's Report*, 1935, p. 97.

‖ *Ber.* 1944, **77**, 220.



There has been considerable controversy[¶] as to whether both α- and β-pinenes (III) and (IV) can yield fenchyl alcohol, but the more recent experiments of Delépine[**] have shown conclusively that it can be prepared from either. For the hydration of pinene to fenchyl alcohol the use of various organic acids has been suggested.[††] The formation of fenchyl alcohol from β-pinene has also been observed to occur when the hydrocarbon is oxidised with hydrogen peroxide in acetic acid solution.[‡‡]

The reduction of fenchyl alcohol with hydriodic acid and red phosphorus at 210–215° yields a hydrocarbon, $C_{10}H_{20}$, the constitution of which has not been determined, but it is apparently identical with that obtained by the reduction of *d*-fenchone under similar conditions.[§§] On oxidation with either chromic acid or nitric acid fenchyl alcohol yields fenchone, the ketone being also formed when the alcohol is distilled over copper.[*]

---

[*] Schmidt and Todenhofer, *Schimmel's Report*, 1937, p. 113; Huckel, Kindler and Wolowski, *loc. cit.*; compare Komppa and Beckmann, *Annalen*, 1936, **522**, 137.

[†] Konovalov, Miller and Timtschenko, *J. Russ. Phys. Chem. Soc.* 1906, **38**, 448.

[‡] Leroide, *Ann. Chim.* 1921 [ix], **16**, 364.

[§] *Compt. rend.* 1887, **105**, 1177; 1897, **125**, 111.

[‖] *Ann. chim.* 1886 [vi], **9**, 578; 1889, **16**, 240; *Compt. rend.* 1891, **113**, 551.

[¶] Compare Barbier and Grignard, *Bull. Soc. chim.* 1909 [iv], **5**, 524.

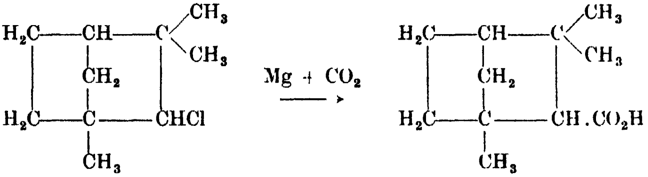
[**] *Compt. rend.* 1924, **178**, 2088; **179**, 175.

[††] Compare *inter al.*, Haller, *Compt. rend.* 1924, **178**, 1936.

[‡‡] Henderson and Chisholm, *J.C.S.* 1924, **125**, 112.

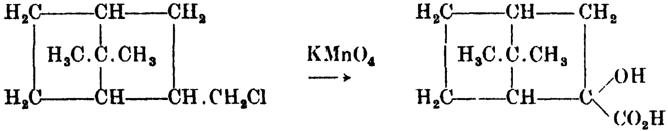
[§§] Wallach, *Annalen*, 1895, **284**, 326.

The replacement of the hydroxyl group in α-fenchyl alcohol by halogen to yield fenchyl chloride (V), which may be carried out either by the action of hydrogen chloride or phosphorus pentachloride, has been the subject of an extremely large number of investigations.[†] There can be no doubt that the reaction proceeds in a most complex manner, yielding a mixture of isomeric fenchyl chlorides, and it is extremely doubtful if the pure fenchyl chloride (V) has actually been prepared from fenchyl alcohol, although the presence of this chloride in the mixture is proved by the experiments of Komppa and Hintikka,[‡] who, by treating the chloride with magnesium and carbon dioxide, prepared the carboxylic acid (VI), m.p. 45–46°.



(V) (VI)

On the other hand, on elimination of hydrogen chloride by the action of bases (aniline, potassium hydroxide, etc.) fenchyl chloride always yields a mixture of the isomeric fenchenes, and it was further observed by Wallach[§] that on oxidation with potassium permanganate it gave hydroxy-α-fenchenic acid (VIII), indicating the presence of a chloride having the structure (VII).



(VII) (VIII)

It would appear to be legitimate to conclude that fenchyl chloride prepared from fenchyl alcohol is a mixture of chlorides derived from the hydrocarbons (IX), (X) and (XI), in which one or the other may predominate, and it is not improbable that, like bornyl, *iso*bornyl chlorides and camphene hydrochloride, they are tautomeric substances. Experimental investigation in this field is hampered by the fact that fenchyl chloride and its isomerides, unlike bornyl chloride, show little tendency to crystallise. It must be mentioned that Aschan* has shown that the liquid chlorides, which are always obtained as a by-product in the preparation of bornyl chloride, contain fenchyl chloride, since, on elimination of hydrogen chloride, a mixture of fenchenes and *cyclo*fenchene is obtained.

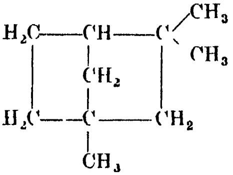
---

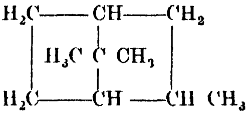
[*] Neave, *J.C.S.* 1912, **101**, 514.

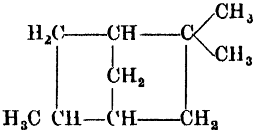
[†] *Inter al.*, Wallach, *Annalen*, 1891, **263**, 148; 1895, **284**, 332; 1898, **302**, 371; 1901, **315**, 299; 1908, **362**, 183; Kondakov and Lutschinin, *J. pr. Chem.* 1900 [ii], **62**, 5; Kondakov and Schindelmeiser, *ibid.* 1903 [ii], **68**, 105; Kondakov, *ibid.* 1909 [ii], **79**, 272; Komppa and Beckmann, *Annalen*, 1934, **509**, 51.

[‡] *Ber.* 1913, **46**, 645.

[§] *Annalen*, 1898, **302**, 382.


(IX)


(X)


(XI)

The marked tendency for fenchyl alcohol to undergo rearrangement is shown further in its behaviour towards dehydrating agents. Under neutral conditions it gives α-fenchene, by a Wagner change, but in the presence of acids the main products are β-fenchene, γ-fenchene, *cyclo*fenchene, and 1-methylsantene, the formation of which has already been discussed on p. 536.

l-*Fenchyl* p-*toluenesulphonate*, m.p. 97–98°, has been described by Huckel, Neunhoeffer, Gercke and Frank.† On treatment with sodium *iso*propoxide it gives a mixture of α- and ζ-fenchenes (see p. 549).

l-*Methyl α-fenchylxanthate* was prepared by Tschugaev‡ and is an oil, but the crystalline *amide* can be obtained by the action of ammonia and melts at 129–130°, $[\alpha]_D$ −78·51° (in benzene). α-Fenchene is the main product formed by distillation of the ester.

A large number of α- and β-fenchyl esters have been prepared by Kenyon and Priston, who have studied their optical properties in great detail and have compared them with similar derivatives of borneol and *iso*borneol.

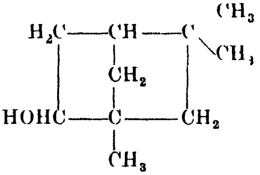
---

* *Ber.* 1907, **40**, 2750; *Annalen*, 1912, **387**, 1.

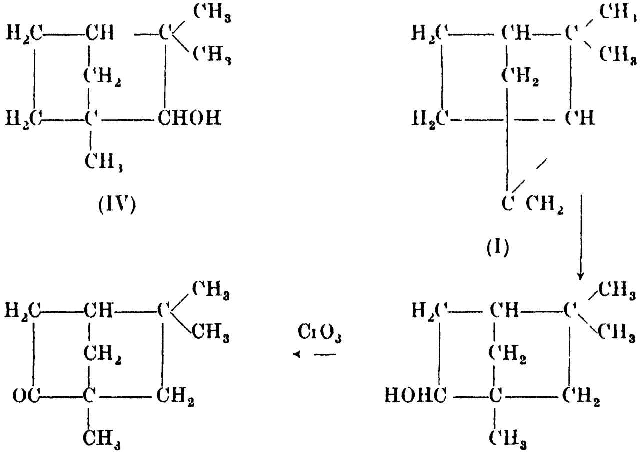
† *Annalen*, 1930, **477**, 99.

‡ *Ber.* 1902, **35**, 2479.

ISO*FENCHYL ALCOHOL*



*iso*Fenchyl alcohol does not occur in nature and the laevorotatory alcohol was first prepared by Bertram and Helle[*] by the hydration of l-α-*fenchene* (I) with sulphuric-acetic acid mixture



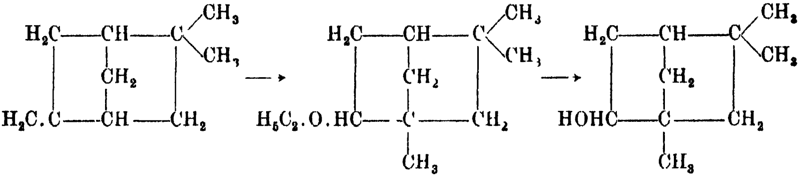
(IV) (I) (III) (II)

It was found that the reaction apparently proceeded solely in the one direction, yielding an alcohol, which after purification through a crystalline hydrogen phthalate melted at 61·5–62°. This alcohol must have the structure represented by (II), since on oxidation it yields iso*fenchone* (III) the proof of the constitution of which is given on p. 581. The most suitable conditions for the preparation of this alcohol from *l*-α-fenchene were determined later by Wallach and Viveck.[†] It is not possible to account for this reaction by a normal Wagner change, since such a transformation would give the structurally isomeric *fenchyl alcohol* (IV); this, however, may be subsequently converted into *iso*fenchyl alcohol through the intermediate formation of *cyclo*fenchene (see p. 538). *l-α-iso*Fenchyl alcohol can be obtained also by the hydration of d-*β-fenchene* (V) with alcohol and sulphuric acid, the *ethyl ether* (VI), b.p. 200–201°, so obtained being readily hydrolysed by water.

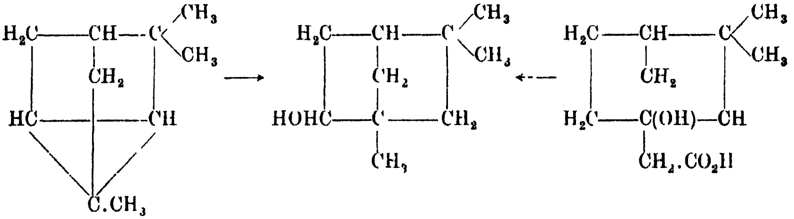
---

[*] *J. pr. Chem.* 1900 [II], **61**, 300.

[†] *Annalen*, 1908, **362**, 191.


(V) (VI) (II)

As mentioned on p. 339, tricyclene on hydration yields borneol (and *iso*borneol) and it is of interest to note that Qvist[*] has shown that d-cyclo*fenchene* (VII) behaves in a similar manner, giving *l-α-iso*fenchyl alcohol.


(VII) (II) (VIII)

*d-α-iso*Fenchyl alcohol was prepared by Wallach[†] by the hydration of *d*-α-fenchene and *l*-β-fenchene and also by the action of dilute sulphuric acid on *nopinol acetic acid* (VIII). The last reaction, also, presumably involves an initial Wagner change into fenchyl alcohol, which then undergoes a further isomerisation.

*l-α-iso*Fenchyl alcohol, which has an odour resembling that of borneol, has m.p. 61·5–62°, b.p. 201–202°, 88°/10 mm., $d^{15°}$ 0·9613, $n_D^{15°}$ 1·4800, $[\alpha]_D$ $-26{\cdot}2°$ (in alcohol), and can be identified as the *phenylurethane*, m.p. 106–107°, the *α-naphthylurethane*,

[*] *Annalen*, 1918, **417**, 278; compare Aschan, *Ber.* 1907, **40**, 2750.

[†] *Annalen*, 1907, **357**, 56; 1908, **363**, 5.

m.p. 114°, the *hydrogen phthalate*, m.p. 155–156°, or the *benzoate*, m.p. 70°.

d-α-*iso*Fenchyl alcohol has m.p. 62–63°, and, according to Kondakov[*] gives a very much higher specific rotation, $[\alpha]_D$ $+45{\cdot}4°$.

dl-α-*iso*Fenchyl alcohol, prepared by Aschan[†] from *cyclo*fenchene, and by Komppa and Beckmann[‡] by hydration of γ-fenchene, has m.p. 42–43°, b.p. 202–203°, $d_4^{20^\circ}$ 0·9533, $n_D^{20^\circ}$ 1·4755, and gives a *phenylurethane*, m.p. 94–95°, and a *hydrogen phthalate*, m.p. 149°.

Evidence for the existence of the stereoisomeric β-*iso*fenchyl alcohol was first obtained by Bertram and Helle, who observed that the alcohol prepared by the reduction of *iso*fenchone with sodium and alcohol was a liquid, which, although it failed to form a phenylurethane, gave a *hydrogen phthalate*, m.p. 110–111°. This, it now appears, was not a homogeneous derivative, since Alder, Stein and Rickert,[§] by hydrogenation of *dl*-isofenchone, have obtained dl-β-iso*fenchyl alcohol*, b.p. 89°/15 mm. (*phthalate*, m.p. 104–105°; *phenylurethane*, m.p. 101°), whilst Schmidt and Todenhöfer[||] have similarly prepared d-β-iso*fenchyl alcohol*, m.p. 8°, b.p. 196–197°, $d_4^{15^\circ}$ 0·952, $n_D^{20^\circ}$ 1·4726, $[\alpha]_D$ + 15·3° (in alcohol), which gave a *hydrogen phthalate*, m.p. 80°, and an α-*naphthylurethane*, m.p. 126°.

Dehydration of *iso*fenchyl alcohol with zinc chloride gives a mixture of fenchenes, in which the β-hydrocarbon predominates.

On oxidation with chromic acid, *iso*fenchyl alcohol (both the α- and β-forms) gives *iso*fenchone, whilst with potassium permanganate it gives the same degradation products as this ketone.

An *iso*fenchyl chloride has been described by Qvist[¶] and by Komppa and Beckmann;[**] it is prepared by the action of phosphorus pentachloride on the alcohol in an inert solvent, and is not homogeneous.[††] (Compare fenchyl chloride, p. 555.) It gives mainly β-fenchene on digestion with *o*-toluidine, whilst with dilute alkali it yields β-*fenchene hydrate*, m.p. 67° (*phenylurethane*, m.p. 101–102°), a stereoisomer of methyl-β-fenchocamphorol (p. 545). l-β-*Fenchene hydrate*, m.p. 68°, $[\alpha]_D^{20}$ −2·6° in benzene (*phenylurethane*, m.p. 92–93°), has been described by Toivonen.[*]

---

[*] *J. pr. Chem.* 1902 [ii], **65**, 227.

[†] *Ber.* 1907, **40**, 2750.

[‡] *Annalen*, **1933**, **503**, 130.

[§] *Ibid.* 1936, **525**, 221.

[||] *Schimmel's Report*, 1937, p. 111.

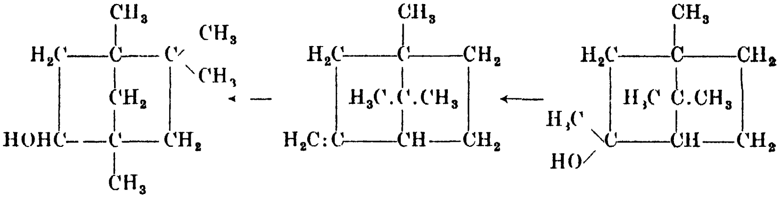
[¶] *Annalen*, 1918, **417**, 278; compare Kondakov, *J. pr. Chem.* 1907 [ii], **75**, 542.

[**] *Annalen*, **1933**, **503**, 130.

[††] Komppa and Beckmann, *Annalen*, 1934, **509**, 51.

Methyl iso*fenchylxanthate* is an oil, but Nametkin[†] has prepared from it a crystalline *amide*, m.p. 69–70°. On distillation the xanthate yields a mixture, consisting mainly of δ-fenchene and *cyclo*fenchene.

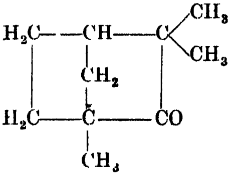
4-*Methyl*iso*fenchyl alcohol* (IX), m.p. 53° (*hydrogen phthalate*, m.p. 146–147°, *phenylurethane*, m.p. 75–76°), is obtained by hydration of 4-*methyl-α-fenchene* (X), itself derived by dehydration of 3-*methylepiborneol* (XI).[‡]



(IX) (X) (XI)

C. KETONES

FENCHONE



In 1890 Schimmel and Co.[§] observed that oil of fennel (from *Foeniculus vulgare*) contained, in addition to anethole, an oxygenated derivative boiling at about 190°, which had a camphoraceous odour. This substance, to which the name *fenchone* was given by Wallach,[‖] was dextrorotatory, and in the following year Wallach[¶] separated its optical enantiomorph from thuja oil

---

[*] *J. pr. Chem.* 1941 [ii], **159**, 70.

[†] *Ibid.* 1923 [ii], **106**, 26.

[‡] Nyman and Kuvaja, *Annalen*, 1939, **538**, 68.

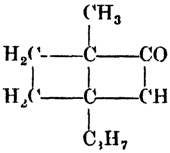
[§] *Schimmel's Report*, 1890, April, p. 20.

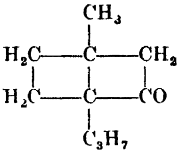
[‖] *Annalen*, 1891, **263**, 129.

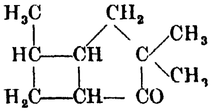
[¶] *Ibid.* 1892, **272**, 102.

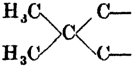
(from *Thuja occidentalis* L.). The only other essential oil in which the ketone occurs in quantity is that derived from *Lavandula dictata.*[*]

After the discovery of fenchone in Schimmel and Co.'s laboratory, its study was undertaken mainly by Wallach and his collaborators, although, as will be seen from the sequel, many important contributions to its chemistry were made by other investigators. Wallach and Hartmann[†] showed that *d*-fenchone had the composition $C_{10}H_{16}O$, and that it was a ketone, since it gave an *oxime*, m.p. 148–149°. It was recognised that fenchone resembled camphor very closely in its properties, and since camphor at the time was regarded as having formula (I), Wallach and Hartmann suggested (II) as a representation of fenchone.


(I)


(II)


(III)

In the following year[‡] this formula was shown to be incorrect, since, on oxidation with potassium permanganate, fenchone gave dimethylmalonic acid, proving the presence in it of the group  $\overset{H_3C}{\underset{H_3C}{>}}C\overset{C-}{\underset{C-}{<}}$; furthermore, it did not contain a $>CH_2$ group adjacent to the carbonyl group as it did not form a hydroxymethylene derivative.[§] Additional proof that camphor and fenchone could not be related to one another as in formulae (I) and (II) was furnished by the fact that, whereas camphor on treatment with dehydrating agents (P_2O_5, etc.) gave *p*-cymene, fenchone gave *m*-cymene. After suggesting various formulae based on (I), but differing in the relative positions of the methyl and *iso*propyl groups, Wallach[‖] advanced a completely different formula (III). This formula had little to recommend it and in the following year Tiemann,[¶] influenced by Bredt's formula for camphor and his own modification thereof, suggested that (IV) was a more probable representation of fenchone. Wallach's

---

[*] *Schimmel's Report*, 1908, April, p. 58.

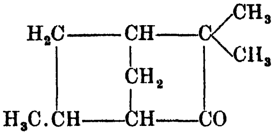
[†] *Annalen*, 1890, **259**, 324.

[‡] *Ibid.* 1891, **263**, 153.

[§] Wallach, *Ber.* 1895, **28**, 34.

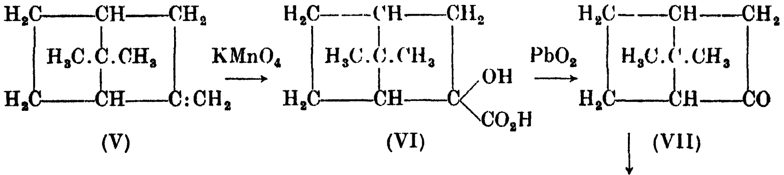
[‖] *Annalen*, 1894, **284**, 342.

[¶] *Ber.* 1895, **28**, 1087.

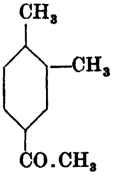


(IV)

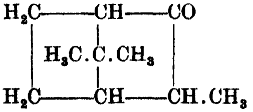
investigation of the oxidation products of *l*-α-fenchene (V) (compare p. 532) led him to reject this formula. This hydrocarbon, which had been prepared from the alcohol resulting by the reduction of fenchone, gave on oxidation *hydroxy-α-fenchenic acid* (VI), from which by the action of lead peroxide the ketone *α-fenchocamphorone* (VII) was prepared. Since the latter gave on oxidation *apocamphoric acid* (VIII), the formula of α-fenchene was obviously represented by (V). On the assumption that no molecular rearrangement occurred in the passage of fenchyl alcohol into α-fenchene Wallach[*] assigned formula (IX) to fenchone.



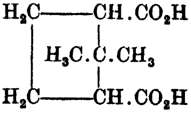
(V) (VI) (VII)



(X)



(IX)



(VIII)

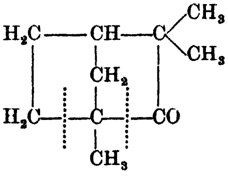
This formula accounted readily for the majority of the reactions of the ketone and received general acceptance. It was supported by the experiments of Gardner and Cockburn,[†] who independently suggested the same formula and who showed that, on prolonged oxidation with nitric acid, the ketone gave a mixture of dimethyltricarballylic, dimethylmalonic and *iso*camphoronic acids. An objection was, however, raised by Marsh,[*] who pointed out that it did not account for the formation of 3:4-dimethylacetophenone (X) by the action of sulphuric acid. This objection was obviously of little weight, since the conversion into the xylene derivative must occur with profound molecular rearrangement.

---

[*] *Annalen*, 1898, **300**, 319.

[†] *J.C.S.* 1898, **73**, 708.

While Wallach's formula for α-fenchocamphorone was rigidly proved, the same did not apply to his fenchone formula. Although α-fenchene was obtained by dehydration of fenchyl alcohol or by the elimination of hydrogen chloride from fenchyl chloride, it was not the only hydrocarbon formed in these reactions, which evidently proceeded in a complex manner. It could not, therefore, be assumed that no molecular rearrangement was involved in its formation. Fenchone was remarkably resistant to oxidation with nitric acid (compare p. 571), reacted only very slowly with semicarbazide, and could not be converted into a carboxylic acid by the action of carbon dioxide in the presence of sodium (compare, however, p. 578). These properties, and others, were inconsistent with the presence of a hydrogen atom in the α-position to a carbonyl group, and in 1905 Semmler[†] suggested in place of the Wallach-Gardner-Cockburn formula the representation (XI), which has since been shown, both analytically and synthetically, to be correct. It will be observed that, if fission is assumed to occur at the dotted lines, the oxidation products isolated by Gardner and Cockburn are accounted for.

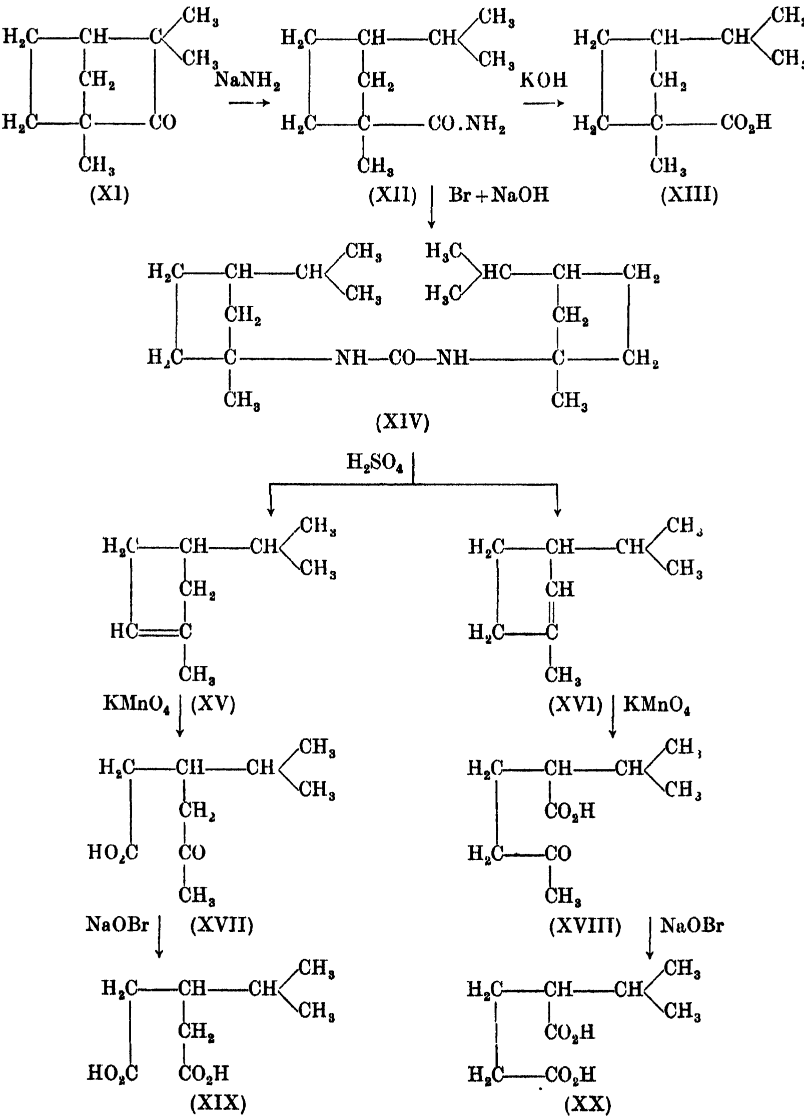


(XI)

One of the main difficulties encountered in the determination of the constitution of fenchone was its great stability towards oxidising agents, which rendered it impossible to carry out a stepwise degradation. An important advance was therefore made when Semmler[‡] observed that, on digesting the ketone with sodamide in benzene solution, ring fission occurred with the formation of d-*fencholamide* (XII), m.p. 94°, from which the corresponding acid, d-*fencholic acid* (XIII), m.p. 18–19°, b.p.

---

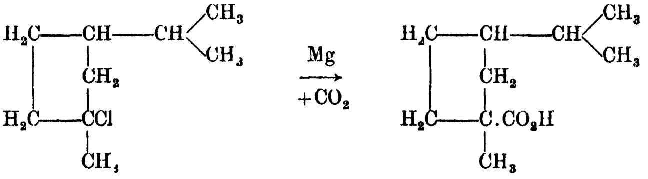
[*] *J.C.S.* 1899, **75**, 1058. [†] *Chem.-Ztg.* 1905, **29**, 1313. [‡] *Ber.* 1906, **39**, 2578.



(XI) (XII) (XIII) (XIV) (XV) (XVI) (XVII) (XVIII) (XIX) (XX)

151–152°/17 mm., could be obtained by hydrolysis with alkali. Later, Wallach* showed that the same acid was formed by fusion of the ketone with potassium hydroxide at 220–240° under pressure.

The reactions of fencholamide were studied in great detail by Bouveault and Levallois,† who effected a partial synthesis of fencholic acid. When *d*-fencholamide was treated with bromine in alkaline solution *difencholylurea* (XIV) was obtained, which on digestion with dilute sulphuric acid gave a hydrocarbon, *apofenchene*, C_9H_{16}, b.p. 143°. This hydrocarbon, from its method of formation, could evidently be represented by either (XV) or (XVI). On oxidation with potassium permanganate a *ketonic acid* was obtained, which had formula (XVII), since it gave on treatment with sodium hypobromite *β*-iso*propylglutaric acid* (XIX). Apofenchene consisted therefore essentially of the hydrocarbon (XV), although as Wallach,‡ who characterised it by the preparation of a *nitrosochloride*, m.p. 115°, showed later, it was not homogeneous, since *α*-iso*propylglutaric acid* (XX) was also obtained by its degradation. By the action of hydrogen chloride on apofenchene Bouveault and Levallois prepared *apofenchyl chloride* (XXI) and from this, by the action of carbon dioxide in the presence of magnesium, fencholic acid (XIII).



(XXI) (XIII)

A comparison of the amides of the synthetic acid, m.p. 104°, with that of fencholamide from *d*-fenchone showed that they were not identical and, since this difference was probably due to stereoisomerism, a second synthesis was devised with the object of preparing *dl*-fencholic acid.

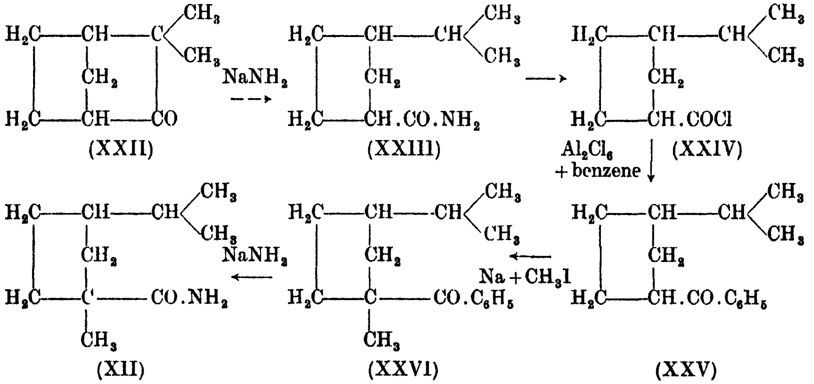
---

* *Annalen*, 1909, **369**, 73.

† *Compt. rend.* 1908, **146**, 181; *Bull. Soc. chim.* 1910 [iv], **7**, 542, 683, 736, 807, 963, 968.

‡ *Annalen*, 1911, **379**, 182.

By fission of the dicyclic ring of camphenilone (XXII) with sodamide, the amide (XXIII) was prepared, and the acid chloride (XXIV) of the acid obtained therefrom by hydrolysis was condensed with benzene by the agency of aluminium chloride. By methylation of the sodium compound of this benzoyl derivative (XXV) with methyl iodide, followed by hydrolysis with sodamide, a fencholamide, m.p. 108°, was obtained. This amide was evidently stereoisomeric with that prepared from apofenchene and also with that derived from *d*-fenchone.* The structural identity of the optically inactive amide derived from *dl*-fenchone (prepared by mixing equal quantities of the *d*- and *l*-amides from *d*- and *l*-fenchones) and the synthetic amide was proved by a comparison of their ureas. *dl*-Difencholylurea, prepared from either of these amides, was obtained in two modifications, m.p. 161–162° and 148°, thus proving their identity.



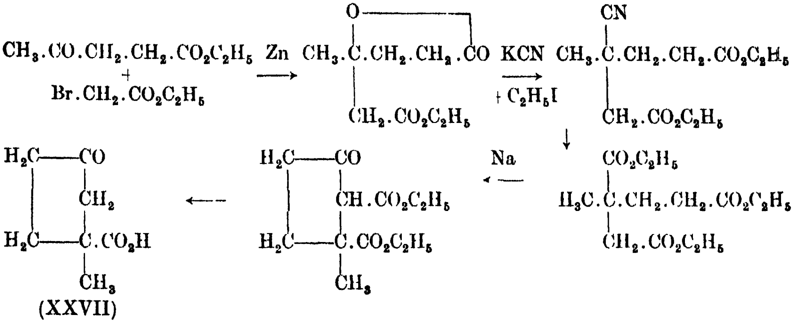
(XXII) (XXIII) (XXIV) (XXV) (XXVI) (XII)

Whilst these ingenious experiments of Bouveault and Levallois provided valuable support for Semmler's formula, complete confirmation was obtained by Ruzicka's† synthesis. The first stage in the synthesis involved that of 1-*methyl*cyclo*pentan*-3-*one carboxylic acid* (XXVII), a substance which had been obtained from *β*-fencholenic acid (see p. 575). The stages of the synthesis are shown in the scheme and do not require comment.

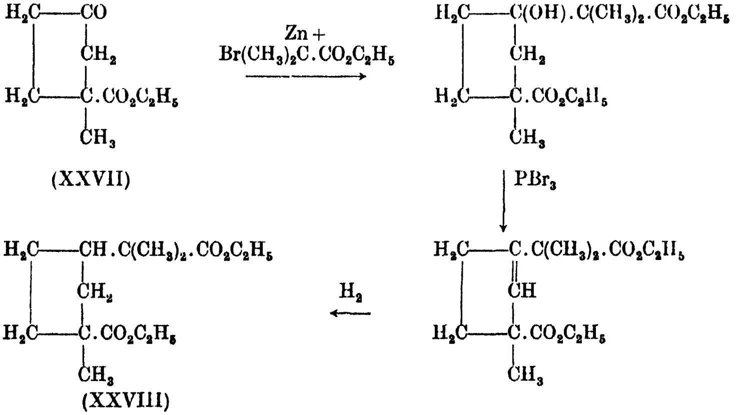
---

* Since the groups attached to the 1 and 3 carbon atoms in fencholamide are different, both *cis*- and *trans*-modifications should be capable of resolution.

† *Ber.* 1917, 50, 1362.


(XXVII)

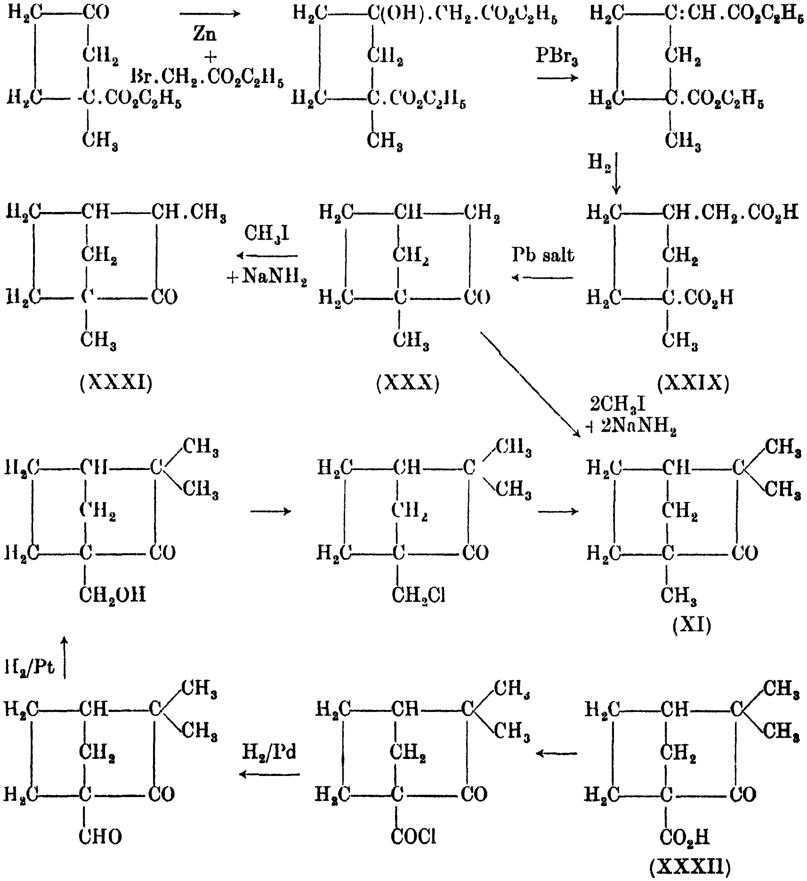
From this ketone Ruzicka prepared the *dicarboxylic ester* (XXVIII), but all attempts to convert this into the dicyclic ketone were unsuccessful.


(XXVII)

(XXVIII)

Since it appeared probable that ring closure was inhibited by the presence of the *gem*-dimethyl group, the related acid (XXIX) was prepared by a similar series of reactions, ethyl bromoacetate being used in the first stage of the reaction in the place of ethyl bromo*iso*butyrate.

When the lead salt of this acid was distilled the dicyclic ketone, 1-*methylnorcamphor* (XXX), b.p. 60–62°/15 mm., *semicarbazone*, m.p. 210–211°, was readily obtained, and this, on methylation with methyl iodide in the presence of sodamide, gave a mixture of *fenchosantenone* (XXXI) and *fenchone* (XI). The two ketones could be readily separated by taking advantage of the fact that, whereas fenchosantenone reacts very readily with semicarbazide, yielding a *semicarbazone*, m.p. 208–209° (*oxime*, m.p. 98–99°), fenchone only reacts with this reagent very slowly. The *dl*-fenchone prepared by this ingenious synthesis was found to be identical in all respects with that prepared by combining equal quantities of *d*- and *l*-fenchones.



(XXXI) (XXX) (XXIX)

(XI)

(XXXII)

A more recent synthesis is due to Komppa and Klami,[*] who obtained the ketone, by the reactions outlined in the lower part of the scheme, from *camphenonic acid* (XXXII). Since this acid may be obtained by cyclisation of camphenic acid, synthesised by Lipp (see p. 299), this also represents a complete synthesis of the ketone.

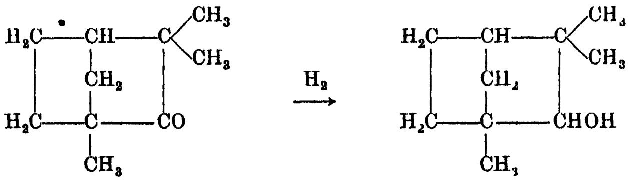
---

[*] *Ber.* 1935, **68**, 2001.

Fenchone is distinguished from other dicyclic ketones by its low boiling-point, and is present in the fraction of oils boiling at 190–200°. It can be comparatively readily freed from impurities by gentle warming with nitric acid, since it is only slowly attacked by this reagent (see below). A complete separation from other ketones can be finally effected by treatment with semicarbazide, since the formation of fenchone semicarbazone requires several days. It can be identified by the preparation of the *oxime*, the optically active form of which melts at 164–165°. The optically active *semicarbazones* melt at 182–183° and the *dl*-form at 172–173°.

Fenchone is an oil possessing an odour reminiscent of that of camphor. It crystallises readily when cooled and melts at 5–6°,[*] b.p. 192–193°, $d^{18°}$ 0·948, $n_D^{18°}$ 1·4635, $[\alpha]_D^{20}$ +66·9°, −64°. Its ultra-violet absorption spectrum has been examined by Henderson, Henderson and Heilbron[†] and has been found to be practically identical with that of acetone; the absorption spectrum of the vapour resembles that of camphor.[‡] The Raman spectrum has been recorded by Dulou[§] and by Jatkar and Padmanabhan.[‖]

The catalytic hydrogenation of *d*-fenchone has been shown[¶] to yield *l*-fenchyl alcohol (XXXIII), though under vigorous conditions fenchane results. By reduction of the ketone with hydriodic acid and red phosphorus at 210–215°, Wallach[**] obtained a saturated hydrocarbon, $C_{10}H_{20}$, but its constitution was



(XI) (XXXIII)

---

[*] Wallach, *Annalen*, 1891, **263**, 131.

[†] *Ber.* 1914, **47**, 881.

[‡] Purvis, *J.C.S.* 1923, **123**, 2516.

[§] *Bull. Inst. Pin*, 1934, p. 214.

[‖] *Ind. J. Phys.* 1936, **10**, 55.

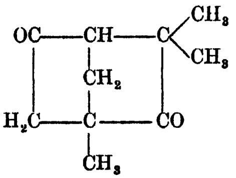
[¶] Ipatiev, *Ber.* 1912, **45**, 3208; Schmidt and Schulz, *Schimmel's Report*, 1935, p. 97; Huckel, Kindler and Wolowski, *Ber.* 1944, **77**, 220.

[**] *Annalen*, 1895, **284**, 326.

not determined. With sodium and alcohol as the reducing agent fenchyl alcohol (XXXIII) is obtained.[*] As was to be anticipated from analogy with camphor and other ketones, the alcohol is a mixture of two stereoisomerides (see p. 553).

Fenchopinacone, $C_{20}H_{34}O_2$, was prepared by Wallach and Wienhaus[†] by heating fenchone with sodium in the absence of air. The *d*- and *l*-forms melt at 97°, $[\alpha]_D$ $+45°$, $-44{\cdot}78°$ (in ethyl acetate), the *dl*- at 104–105°.

Fenchone is slowly oxidised by air in the presence of sunlight[‡] with evolution of carbon monoxide and formation of a *glycol*, $C_{10}H_{18}O_2$, m.p. 138–139°, *diphenylurethane*, m.p. 206°. The constitution of this glycol has not been determined. On oxidation with chromic acid, *d*-fenchone behaves in a similar manner to camphor,[§] yielding a *diketone*, b.p. 108°/10·5 mm., $[\alpha]_D$ $+75{\cdot}78°$ (in benzene), *monophenylhydrazone*, m.p. 149–150°, *monosemicarbazone*, m.p. 222–223°, which is probably represented by (XXXIV); if this is so, it should be identical with a diketone, m.p. 36° (*di-semicarbazone*, m.p. 243°), obtained by Reinartz and Zanke[||] by the oxidation of the mixture of hydroxyfenchones isolated from the urine of dogs fed on fenchone.



(XXXIV)

Fenchone is not attacked by a cold solution of potassium permanganate, but when warmed with this reagent it is slowly oxidised, yielding a mixture of dimethylmalonic, oxalic and acetic acids.[¶]

By the action of dilute nitric acid (*d* 1·075) under pressure at 120–130° Konovalov[**] obtained a mixture of secondary and tertiary nitrofenchones which have since been studied in greater detail by Nametkin and his collaborators.* sec.-*Nitrofenchone*, m.p. 88°, $[\alpha]_D$ $-42{\cdot}88°$, yielding a *bromide*, m.p. 53°, is probably represented by (XXXV), since it gives on treatment with tin and hydrochloric acid the *ketonic acid* (XXXVI), m.p. 79–80°, *semicarbazone*, m.p. 188°. tert.-*Nitrofenchone*, which must have formula (XXXVII), yields on reduction a *diketone*, b.p. 126·5–127°/11 mm., $[\alpha]_D$ $-45{\cdot}59°$, *disemicarbazone*, m.p. 220°, *dioxime*, m.p. 123–124°, which may be either (XXXVIII) or (XXXIX), of which the latter is considered the more probable, since on reduction it gives a *glycol* (XL), b.p. 151–152°/11 mm., which is readily converted into an oxide.

---

[*] Wallach, *Annalen*, 1891, **263**, 143; Bertram and Helle, *J. pr. Chem.* 1900 [ii], **61**, 294; Gardner and Cockburn, *J.C.S.* 1898, **73**, 276; Schmidt and Schulz, *loc. cit.*

[†] *Annalen*, 1909, **369**, 68.

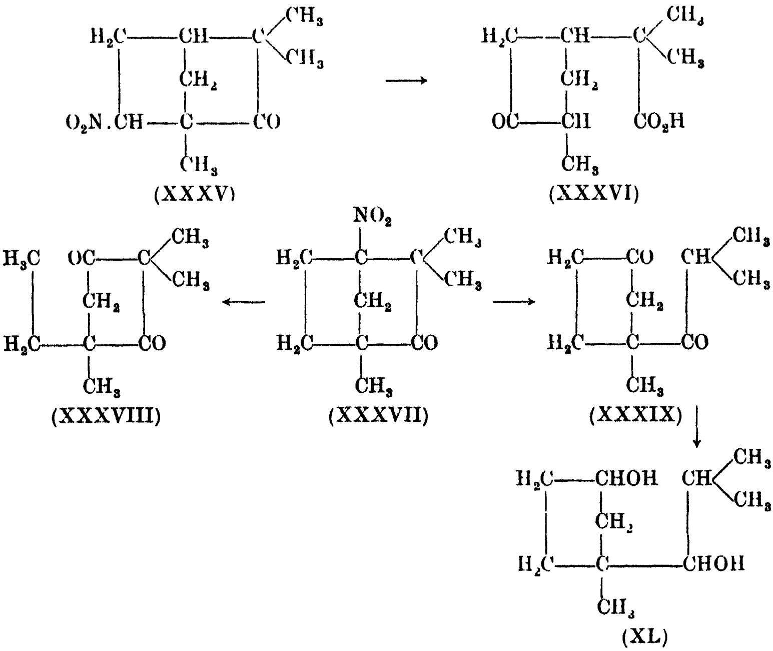
[‡] Ciamician and Silber, *Ber.* 1910, **43**, 1346.

[§] Bredt, *J. pr. Chem.* 1923 [ii], **106**, 338.

[||] *Ber.* 1936, **69**, 2259.

[¶] *Annalen*, 1891, **263**, 134.

[**] *J. Russ. Phys. Chem. Soc.* 1903, **35**, 953.



(XXXV) (XXXVI)

(XXXVIII) (XXXVII) (XXXIX)

(XL)

When fenchone is warmed on the water bath with concentrated nitric acid it is slowly oxidised, although, as Gardner and Cockburn† showed, even after six days 50 per cent. of the ketone can be recovered. As mentioned on p. 563 the products of the oxidation are *iso*camphoronic, αα-dimethyltricarballylic, dimethylmalonic and *iso*butyric acids.

---

* Nametkin and Chochrjakova, *J. Russ. Phys. Chem. Soc.* 1922, **54**, 163; Nametkin, Lubovcova and Chochrjakova, *ibid.* p. 169; Nametkin, *J. pr. Chem.* 1922 [II], **108**, 29.

† *J.C.S.* 1898, **73**, 708.

At the ordinary temperature fenchone reacts with the halogens to give crystalline addition compounds, which, although stable in the absence of moisture, readily pass into the parent ketone on treatment with alkali.[*] Czerny[†] found, however, that a *bromofenchone*, b.p. 131–134°/18 mm., d^{12} 1·348, $n_D^{12°}$ 1·5101, $[\alpha]_D$ +11·6°, could be prepared by heating *d*-fenchone with bromine at 100°. This product is probably a mixture;[‡] according to Semmler and Bartelt[§] it contains 6-bromofenchone (XLI), since by the action of alcoholic potassium hydroxide it is converted into γ-fencholenic acid, b.p. 145–146°/10 mm., $[\alpha]_D$ +52·30°. This acid Semmler and Bartelt consider to be the *cyclo*butane acid (XLII), since on ozonolysis it gives a *ketonic acid* (XLIII), b.p. 185–187°/10 mm., *semicarbazone*, m.p. 192°. No direct evidence of the presence in these acids of the *cyclo*butane or *cyclo*butanone ring structure is available and their constitution cannot be regarded as established. γ-Fencholenic acid is very unstable and on standing slowly changes into *α-fencholenic acid* (XLIV) (see p. 574), the amide of which is formed when the ammonium salt of γ-fencholenic acid is heated under pressure at 180°. The isomerisation of γ-fencholenic acid to α-fencholenic acid resembles that of infracampholenic acid, which also has an exocyclic ethylenic linkage, to *iso*lauronolic acid (compare p. 437).

If fenchone is treated with bromine in the presence of phosphorus pentabromide, then, in addition to substitution, replacement of the oxygen atoms in the carbonyl group occurs with the formation of a *tribromofenchane*, b.p. 181–183°/18 mm. Assuming no molecular rearrangement to have occurred, this probably has formula (XLV).

Fenchone is not attacked by the halogen acids, whilst on treatment with phosphorus pentachloride Gardner and Cockburn[||] showed that a complicated reaction took place yielding a mixture of products which, according to Komppa and Hasselström[*] contains *fenchone dichloride*, b.p. 105–107°/11 mm., and a *chlorofenchene*, m.p. 45–46°. When the ketone is heated with phosphorus pentoxide *m*-cymene is formed,[†] whilst by the action of concentrated sulphuric acid at 80° Marsh[‡] obtained 3·4-dimethylacetophenone.

---

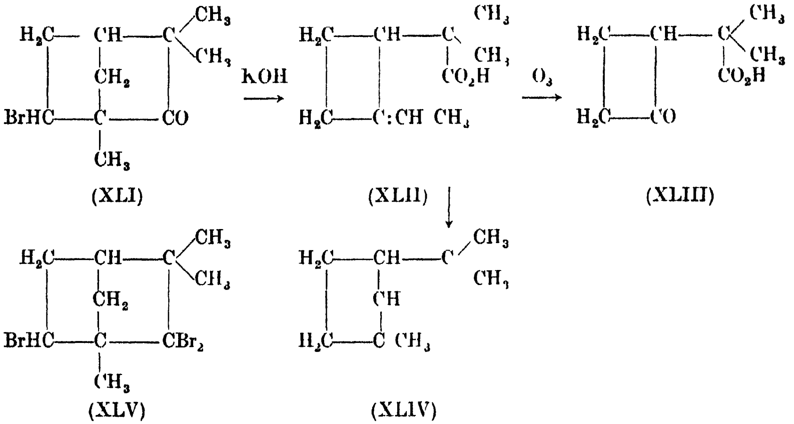
[*] Wallach, *Annalen*, 1890, **259**, 326; 1891, **263**, 132; 1895, **284**, 342; compare Briusova, *J. Gen. Chem. Russ.* 1940, **10**, 1462.

[†] *Ber.* 1900, **33**, 2291; compare Balbiano, *Gazzetta*, 1900, **30**, II, 382.

[‡] Briusova, *loc. cit.*

[§] *Ber.* 1907, **40**, 1432.

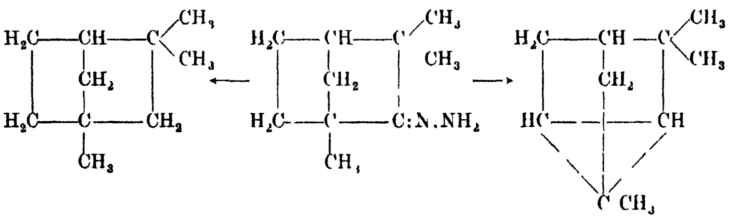
[||] *J.C.S.* 1897, **71**, 1151; 1898, **73**, 704.



(XLI) (XLII) (XLIII)

(XLV) (XLIV)

d-Fenchonehydrazone (XLVI), m.p. 56–57°, b.p. 230–231°, was shown by Kishner[§] to give *fenchane* (XLVII) when distilled with potassium hydroxide, the same hydrocarbon being obtained by the action of sodium ethoxide at 140°.[‖] On oxidation with mercuric oxide in the presence of alkali it yields d-cyclo*fenchene* (XLVIII).[¶]



(XLVII) (XLVI) (XLVIII)

---

[*] *Annalen*, 1933, **502**, 272.

[†] Wallach, *Annalen*, 1893, **275**, 157; 1895, **284**, 324.

[‡] *J.C.S.* 1899, **75**, 1058; compare Zaugg, *J. Amer. C.S.* 1945, **67**, 1861.

[§] *J. Russ. Phys. Chem. Soc.* 1911, **43**, 582.

[‖] Wolff, *Annalen*, 1912, **394**, 96.

[¶] G.P. 353933.

Fenchoneoxime (XLIX) (p. 575) was first prepared by Wallach,[*] the *d*- and *l*-forms melting at 164–165°, $[\alpha]_D \pm 47°$ (in alcohol) and the *dl*- at 158–160°. Delépine[†] has prepared a second oxime, d-*fenchone-β-oxime*, m.p. 123°, $[\alpha]_D + 129{\cdot}3°$. This oxime is labile, and on warming to 170–180°, or even by the evaporation of its alcoholic solution, it passes into the ordinary oxime, m.p. 164–165°. Fenchoneoxime is insoluble in alkalis and, like camphoroxime, it cannot be reconverted into the parent ketone by acid hydrolysis. When it is warmed with dilute mineral acids it yields a mixture of two nitriles, which were first prepared by Wallach and carefully studied by him,[‡] but their actual separation was first effected by Cockburn.[§]

If fenchoneoxime is warmed with dilute sulphuric acid an oil is obtained which, although it boils within comparatively narrow limits, 214–219°, is a mixture of two nitriles which cannot be separated by fractional distillation. Separation can, however, be effected by taking advantage of the fact that one of the nitriles, *β-fencholenonitrile* (L), is readily hydrolysed by alcoholic potassium hydroxide to the corresponding acid, *β-fencholenic acid* (LI), whilst the other nitrile, α-fencholenonitrile (LII) or (LIIa), is more stable and yields a crystalline *amide* (LIII) or (LIIIa), m.p. 113–114°, from which the acid, *α-fencholenic acid* (LIV) or (LIVa), can be obtained by prolonged hydrolysis with alkali.

The position of the ethylenic linkage in α-fencholenic acid, b.p. 136–138°/12 mm., $d^{16°}$ 1·0069, $[\alpha]_D + 30{\cdot}73°$, has not been determined, but it is generally assumed to have either formula (LIV) or (LIVa). It would appear to behave abnormally on oxidation with ozone, since Semmler and Bartelt[‖] showed that it gave an oil which did not contain a carbonyl group. On catalytic hydrogenation it yields the saturated acid, *dihydro-α-fencholenic acid* (LV), whilst, when dissolved in cold concentrated sulphuric acid, the *lactone* (LVI), m.p. 77–78°, is formed, which yields on reduction the glycol (LVII), m.p. 58–60°.

---

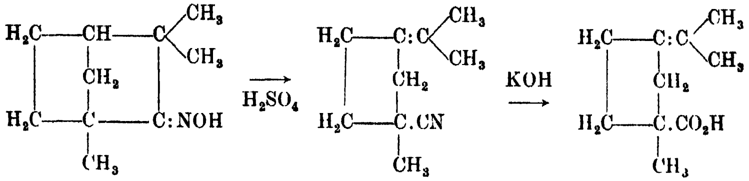
[*] *Annalen*, 1891, **263**, 136; 1893, **272**, 104; 1901, **315**, 278; compare Rimini, *Gazzetta*, 1896, **26**, II, 502; Cockburn, *J.C.S.* 1899, **75**, 503.

[†] *Compt. rend.* 1924, **178**, 1721.

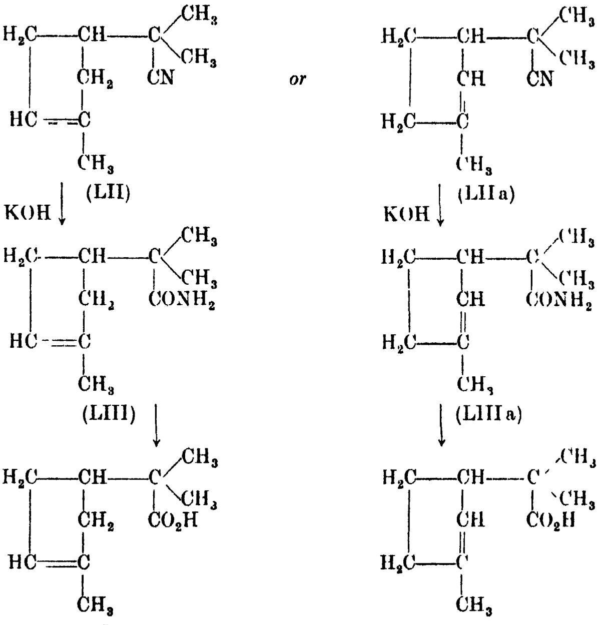
[‡] *Annalen*, 1890, **259**, 329; 1892, **269**, 332; 1901, **315**, 278; 1911, **379**, 182.

[§] *J.C.S.* 1899, **75**, 501.

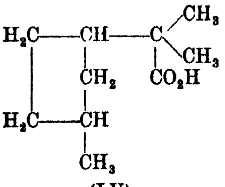
[‖] *Ber.* 1907, **40**, 432.



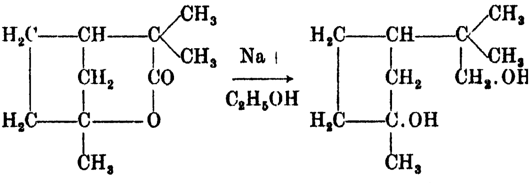
(XLIX) (L) (LI)



(LII) (LIIa) (LIII) (LIIIa) (LIV) (LIVa)

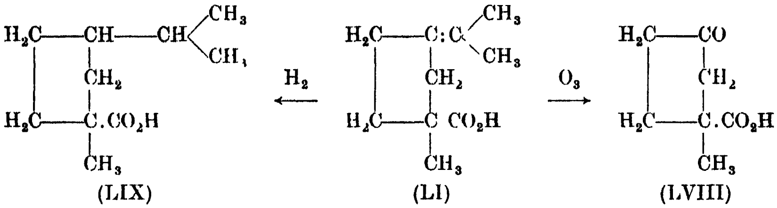


(LV)

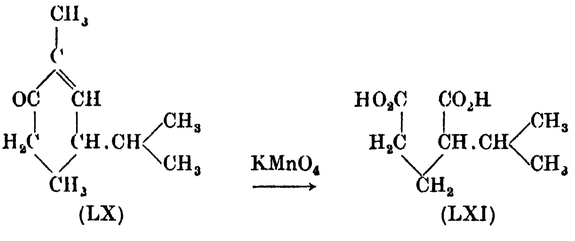


(LVI) (LVII)

Although the constitution of α-fencholenic acid remains uncertain, that of the *β-acid* (LI), m.p. 72–73°, $[\alpha]_D$ +19·64° (in alcohol), *amide*, m.p. 86·5–87·5°, has been definitely established, since, on ozonolysis, it gives 1-*methyl*cyclo*pentan*-3-*one carboxylic* *acid* (LVIII),[*] which has been synthesised by Ruzicka (compare p. 567). On catalytic hydrogenation it yields *fencholic acid* (LIX), identical with the acid prepared by the fusion of fenchone with alkali (p. 565).



The action of nitrous acid on *d*-fenchoneoxime has been investigated by Rimini[†] and by Tiemann and Mahla,[‡] who have shown that a mixture of *pernitrosofenchone*, $C_{10}H_{16}O_2N_2$, and *fenchoneimine*, $C_{10}H_{16}:NH$, is obtained. The former, m.p. 66–67°, is converted by cold alcoholic ammonia into iso*pernitrosofenchone*, m.p. 88°, whilst with cold concentrated sulphuric acid it gives the so-called iso*camphor*, which Wallach[§] has shown, as was suggested by Rimini, to be 1-methyl-3-*iso*propyl-Δ^1-*cyclo*hexen-6-one (LX), since on oxidation with potassium permanganate it gives α-*iso*propylglutaric acid (LXI). Pernitrosofenchone, on heating to 150–160°, gives a mixture of α- and *β-fencholenonitriles* (L), and (LII) or (LIIa).[‖]



d-Fenchoneimine (LXII), which is readily separable from pernitrosofenchone owing to the sparing solubility of its nitrate, is an oil, b.p. 82°/15 mm., $[\alpha]_D$ +76·3°. When air is led through the imine at 105° for 36 to 48 hours ring fission occurs (compare camphorimine, p. 442), a mixture of *nitriles* of dihydro-α-fencholenic acid (LXIII), b.p. 98–104°/23 mm., and hydroxydihydro-α-fencholenic acid (LXIV), b.p. 154°/23 mm., being obtained. The former gives on hydrolysis dihydro-α-fencholenic acid, identical with the acid prepared by Wallach[*] by the catalytic hydrogenation of α-fencholenic acid (p. 574). Hydrolysis of the hydroxynitrile gives a *hydroxy acid*, m.p. 113–114°, from which a lactone, m.p. 72°, can be prepared. This lactone, if not identical with, must be a stereoisomeride of that prepared by Semmler and Bartelt[†] from α-fencholenic acid by the action of concentrated sulphuric acid (compare p. 574).

---

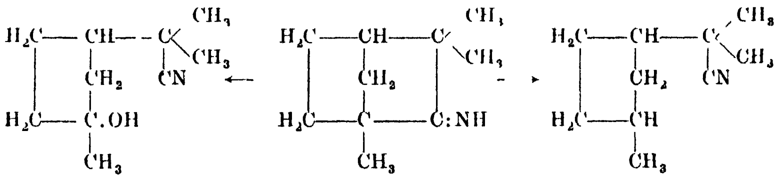
[*] Semmler and Bartelt, *Ber.* 1907, **40**, 432.

[†] *Gazzetta*, 1896, **26**, II, 505.

[‡] *Ber.* 1896, **29**, 2818.

[§] *Annalen*, 1911, **379**, 217.

[‖] Gandini, *Gazzetta*, 1942, **72**, 232.


(LXIV) (LXII) (LXIII)

By the reduction of *d*-fenchoneoxime with sodium and alcohol Wallach[‡] prepared *l-fenchylamine*, b.p. 195°, $[\alpha]_D$ $-24{\cdot}89°$, the enantiomorph being obtained from *l*-fenchoneoxime. This amine can be prepared also by heating together a mixture of fenchone, ammonium formate, and formamide.[§] It has an odour resembling that of piperidine and, as usually prepared, is a mixture of the stereoisomeric α- and β-forms. The *dl*-fenchylamine, so obtained, has b.p. 190–191°, $d_{20}^{20°}$ 0·8971, $n_D^{25°}$ 1·4711 (*benzoyl* derivative, m.p. 131–133°). Huckel, Kindler and Wolowski[‖] have found that a mixture of approximately equal amounts of α- and β-fenchylamines is obtained by hydrogenation of fenchoneoxime over Raney nickel. Separation of the components was carried out through the crystalline formyl and benzoyl derivatives, and gave *α-fenchylamine* (*formyl* derivative, m.p. 115°, $[\alpha]_D^{20°}$ $-64°$ in alcohol; *acetyl*, m.p. 99°, $[\alpha]_D^{20°}$ $-60°$; *benzoyl*, m.p. 91°, $[\alpha]_D^{20°}$ $-26°$) and *β-fenchylamine* (*formyl* derivative, m.p. 124°, $[\alpha]_D^{20°}$ $+60°$; *acetyl*, m.p. 159°, $[\alpha]_D^{20°}$ $+62°$; *benzoyl*, m.p. 164°,

---

[*] *Annalen*, 1911, **379**, 182.

[†] *Ber.* 1906, **39**, 2853; 1907, **40**, 438.

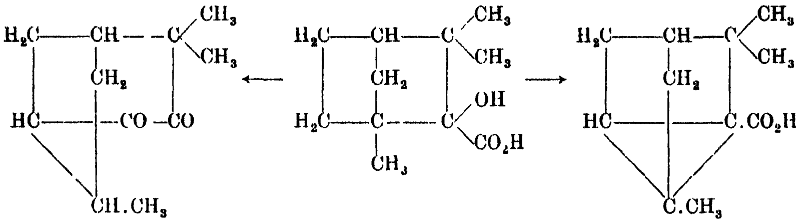
[‡] *Annalen*, 1891, **263**, 140; 1892, **269**, 358; 1893, **272**, 105; **276**, 318.

[§] Ingersoll, Brown, Kim, Beauchamp and Jennings, *J. Amer. C.S.* 1936, **58**, 1810.

[‖] *Ber.* 1944, **77**, 220.

$[\alpha]_D^{20^\circ}$ $+43^\circ$). With nitrous acid *l*-fenchylamine reacts in a somewhat complicated manner, yielding a mixture of cineole, *d*-limonene, dipentene, α- and β-fenchyl alcohols, and *l*-α-fenchene, the *d*-amine behaving in a similar manner.[*]

Since fenchone does not contain a $—CH_2$-group adjacent to the carbonyl group it does not form a sodium derivative, but it was observed by Wallach[†] that, when carbon dioxide was passed into an ethereal solution of the ketone containing sodium wire, an interesting reaction took place with the formation of two isomeric hydroxy-acids, α- and *β-fenchocarboxylic acids*. These two acids are probably *cis*- and *trans*-modifications of the acid having the formula (LXV), since on oxidation with potassium permanganate the parent ketone is formed.


(LXVII) (LXV) (LXVI)

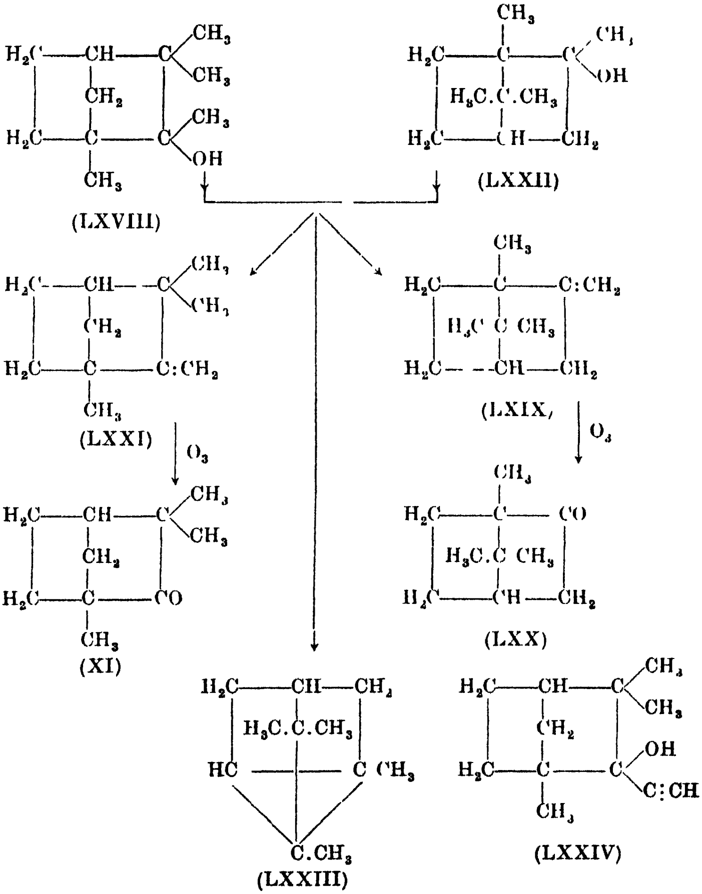
α-Fenchocarboxylic acid, which is known in both the *d*- and *l*-modifications, melts at 141–142°, $[\alpha]_D$ ± 11·28°, *dl*-, m.p. 91–92°, and it can be distilled without decomposition under diminished pressure, but at the ordinary pressure decomposes with loss of water and formation of *anhydrofenchocarboxylic acid*, m.p. 175°. This acid is probably the *cyclo*fenchenecarboxylic acid (LXVI). In addition to this acid a yellow diketone, *carbofenchonone*, m.p. 96°, is formed, which can, however, be obtained in a better yield by the distillation of the lead salt of α-fenchocarboxylic acid. This ketone, which possibly has formula (LXVII), gives an *oxime*, m.p. 108°, and a *dioxime*, m.p. 198–199°. There can be no doubt that the carbonyl groups are in the 1:2-position, since it yields a *quinoxaline* derivative, m.p. 121–122°. A further study of the properties of this diketone would be of interest.

---

[*] Wallach, *Annalen*, 1908, **362**, 177; Hückel and Wolowski, *Chem. Ber.* 1947, **80**, 39.

[†] *Annalen*, 1890, **259**, 326; 1895, **284**, 327; 1898, **300**, 294; 1901, **315**, 276.

β-Fenchocarboxylic acid, of which only the dextrorotatory form is known, melts at 76–77° and is much less stable than the α-acid; it passes very readily into the anhydro-acid. It is of interest that this acid can be prepared by digestion of carbofenchonone with alkali and it can be converted into the diketone by distillation of its lead salt.



The action of methyl magnesium iodide on *d*-fenchone was first investigated by Zelinski* and later by Wallach and Wienhaus.† The reaction proceeds normally with the formation of α- (or tert.-) *methylfenchyl alcohol* (LXVIII), m.p. 61°, b.p. 215–216°, $[\alpha]_D$ +1·7° (in ether). On dehydration with potassium hydrogen sulphate, methylfenchyl alcohol yields a mixture of hydrocarbons, which Ruzicka has shown to consist essentially of 1-*methyl-α-fenchene* (LXIX) and α-methylcamphene (LXXI), since on ozonisation camphor (LXX) and fenchone (XI) are formed. In addition, the tricyclic hydrocarbon (LXXIII) is present.[*] The same mixture of hydrocarbons is also obtained by the dehydration of *tert.*-methylborneol (LXXII).[†]

---

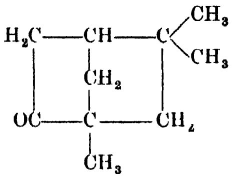
* *Ber.* 1901, **34**, 2883.

† *Annalen*, 1907, **353**, 219.

On condensation with acetylene, in the presence of sodium, fenchone gives the *acetylenic carbinol* (LXXIV), b.p. 89°/12 mm.[‡]

Tardy[§] has prepared a number of additive compounds of fenchone with various phenols and also with chloral.

ISO*FENCHONE*



l-*iso*Fenchone was first described by Bertram and Helle,[‖] who obtained it by the oxidation of *l*-*iso*fenchyl alcohol with chromic acid mixture, the dextrorotatory isomeride being prepared some years later by Wallach[¶] by the oxidation of *d*-*iso*fenchyl alcohol.

The formula, now known to represent correctly the constitution of *iso*fenchone, was originally suggested by Semmler[**] and was based on the following considerations. *iso*Fenchyl alcohol, from which *iso*fenchone is obtained, results from the hydration of α-fenchene (I). Addition of water to this hydrocarbon, with the accompanying Wagner rearrangement, can proceed in two

[*] Bredt and Savelsberg, *J. pr. Chem.* 1918 [ii], **98**, 97; compare Bredt-Savelsberg and Buchkremer, *Ber.* 1931, **64**, 600.

[†] Compare Nametkin and Brüssoff, *Annalen*, 1927, **459**, 144. The dehydration of tert.-*methylepiborneol* to give 4-methyl-α-fenchene has been reported by Nyman and Kuvaja, *Annalen*, 1939, **538**, 68.

[‡] Rupe and Kuenzy, *Helv. Chim. Acta*, 1931, **14**, 708; compare Dulou, *Bull. Inst. Pin*, 1934, pp. 164, 178, 197; Hurd and Christ, *J. Amer. C.S.* 1937, **59**, 118.

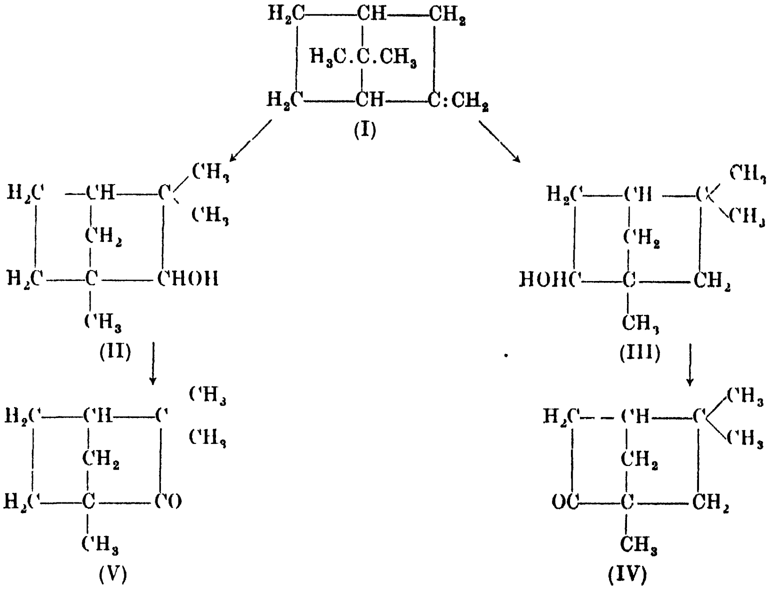
[§] *Bull. Soc. chim.* 1902 [iii], **27**, 605.

[‖] *J. pr. Chem.* 1900 [ii], **61**, 303.

[¶] *Annalen*, 1907, **357**, 56; 1908, **363**, 4.

[**] *Die Ätherischen Öle*, 1906, III, 549.

directions to yield the alcohols (II) and (III).[*] If Semmler's formula[†] for *fenchone* (V) (p. 564) was correct, then (II) corresponded to *fenchyl alcohol* and (III) must represent *iso*fenchyl alcohol, from which it followed that *iso*fenchone was (IV).



The investigations of Wallach, Aschan and their collaborators, which must now be considered, have shown Semmler's formula to be correct. Wallach[‡] found that, when *iso*fenchone was oxidised with potassium permanganate in alkaline solution, a dibasic acid, iso*fenchocamphoric* acid, $C_{10}H_{16}O_4$, was obtained, whilst by fusion with potassium hydroxide at 220–240° Wallach and Homberger[§] prepared a monobasic acid, iso*fencholic acid*, $C_{10}H_{18}O_2$. Accepting Semmler's formula for *iso*fenchone, these reactions can be formulated in accordance with the following scheme, when *iso*fenchocamphoric acid will be (VI) and *iso*fencholic acid (VII) or (VIII).

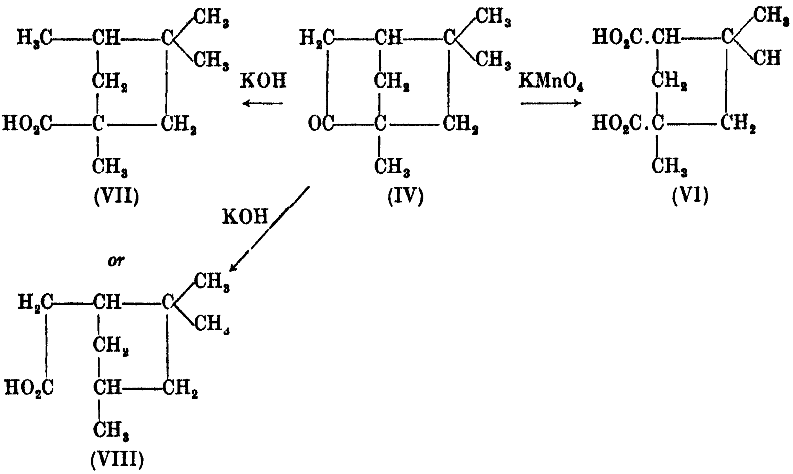
---

[*] It should be noted that a true Wagner rearrangement can lead only to the alcohol (II). The isomer (III) may, however, be derived from (II) through the intermediate formation of *cyclo*fenchene (compare p. 538).

[†] *Chem.-Ztg.* 1905, **29**, 1913.

[‡] *Annalen*, 1908, **362**, 191; **363**, 5.

[§] *Ibid.* 1909, **369**, 97.



(VII) (IV) (VI)

or

(VIII)

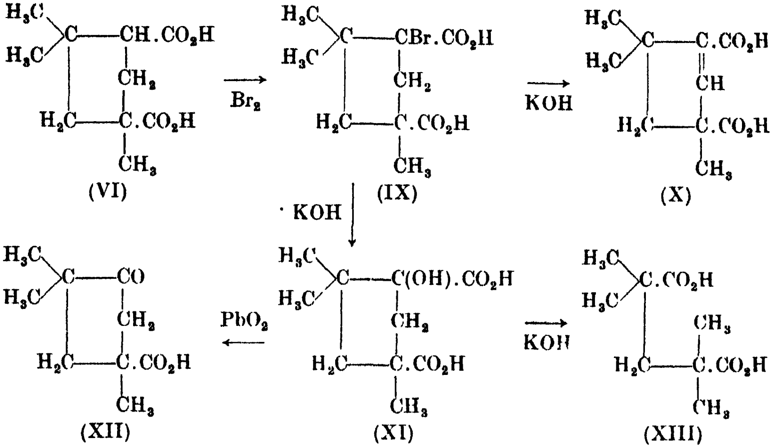
Aschan[*] studied the properties of *iso*fenchocamphoric acid in very great detail. The acid prepared by Wallach was found to be the *cis*-modification, since it readily gave an anhydride and it could be converted into the *trans*-form by heating with acetic-hydrochloric acid at 180° for some hours. The following constants have been observed for the *cis*- and *trans*-acids.

	m.p.	$[\alpha]_D$
cis-d- and *l*-acids	158–159°	+14·58°, −14·54°
cis-dl-acid	174–175°	± 0°
cis-d- and *l*-anhydrides	98°	±13·45°
cis-dl-anhydride	95–96°	± 0°
trans-d- and *l*-acids	149–150·5°	+4·16°, −4·19°
trans-dl-acid	173–174°	± 0°

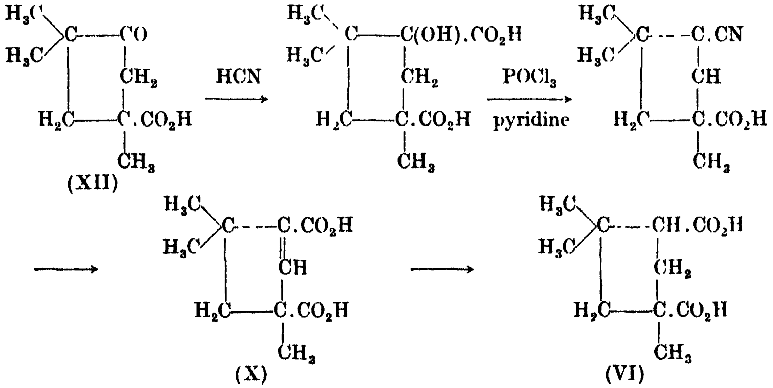
On bromination, *cis-dl-iso*fenchocamphoric acid gave only a monobromo-acid, cis-dl-*α-bromo*iso*fenchocamphoric acid* (IX), obtained in two stereoisomeric modifications, m.p. 208–210° and 160–162°, which indicated that *iso*fenchocamphoric acid had only one hydrogen atom in the α-position to a carboxyl group. By treatment of *cis-dl*-α-bromo*iso*fenchocamphoric acid with alkali, an unsaturated acid, *dehydro*iso*fenchocamphoric acid* (X), m.p. 190–191°, and a hydroxy acid, cis-dl-*α-hydroxy*iso*fenchocamphoric acid* (XI), m.p. 185–186°, were obtained. The latter was shown to contain a hydroxyl group in the α-position to a carboxyl group, since by oxidation with lead peroxide it was

---

[*] *Annalen*, 1912, **387**, 1; compare Sandelin, *ibid.* 1913, **396**, 285.



converted into a ketonic acid, iso*fenchocamphononic acid* (XII), m.p. 68–70°, *semicarbazone*, m.p. 216–217°. Its constitution was conclusively established by fusion with potassium hydroxide, when it gave *ααγγ-tetramethylglutaric acid* (XIII) and formic acid. The structure of *iso*-fenchocamphononic acid (XII) has been confirmed by synthesis,* and more recently this acid has been converted into *iso*fenchocamphoric acid by the route outlined below:†

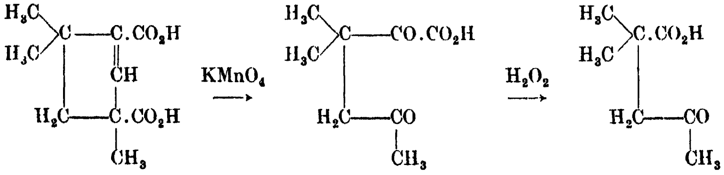


---

* Bardhan and Ganguly, *J.C.S.* 1936, p. 1852; Ranganathan, *J. Ind. C.S.* 1937, **14**, 264.

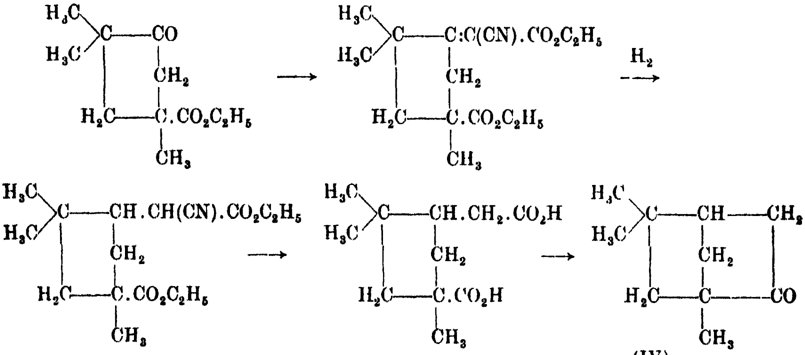
† Swaminathan, Mukherji and Bardhan, *J.C.S.* 1949, p. 192. An alternative synthesis of *iso*fenchocamphoric acid is also described in this paper.

The reactions of dehydro*iso*fenchocamphoric acid (X), the synthesis of which is included in the above scheme, have been studied in some detail by Toivonen.* The acid, *d*- and *l*-forms, m.p. 170–171°, *dl*-, m.p. 190–191°, does not yield an anhydride, but its constitution is proved by its oxidation with potassium permanganate to *αδ-diketo-ββ-dimethylhexoic acid* (XIV), which, by the action of hydrogen peroxide, gave *mesitonic acid* (XV).



(X) (XIV) (XV)

The synthesis of *dl-iso*fenchone has recently been reported by Mukherji and Bardhan.† The ethyl ester of *iso*fenchocamphononic acid was condensed with cyanoacetic ester and the product, after reduction, was hydrolysed to the saturated homo*iso*fenchocamphoric acid; the latter, on cyclisation by pyrolysis in the presence of barium hydroxide, gave *iso*fenchone (IV). The reactions are outlined below:



(IV)

*iso*Fenchone can be characterised either by the preparation of the *semicarbazone*, *d*- and *l*-, m.p. 221–222°, *dl*-, m.p. 223–224°,‡

---

[*] *Annalen*, 1919, **419**, 176.

[†] *J.C.S.* 1949, p. 197.

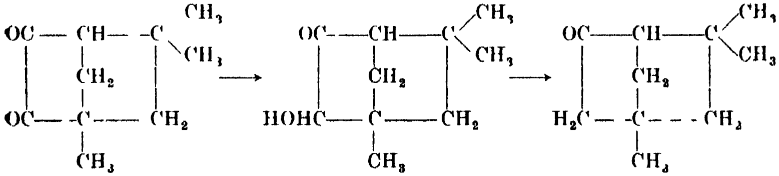
[‡] Wallach and Virck, *Annalen*, 1908, **362**, 194.

the *oxime*, *d*- and *l*-, m.p. 82°, *dl*-, m.p. 133°, or the *hydrazone*, m.p. 111–112°.*

l-*iso*Fenchone is an oil with an odour resembling that of camphor; when cooled to a low temperature it solidifies to an amorphous solid. It has b.p. 193–194°, $d_{4°}^{15°}$ 0·949, $n_D^{20°}$ 1·4619, $\alpha_D^{20°}$ $-9{\cdot}3°$.

When *iso*fenchone is hydrogenated, or reduced with sodium and alcohol, it yields a stereoisomeric mixture of *iso*fenchyl alcohols (see p. 558).

The oxidation of *iso*fenchone with potassium permanganate has already been considered above. With selenium dioxide, the ketone gives iso*fenchone quinone* (XVI), *dl*-, m.p. 49–50°, *l*-, m.p. 69–70°, $[\alpha]_D$ $-12{\cdot}8°$,† which on further oxidation gives *iso*fenchocamphoric acid. Reduction of the *l*-quinone with zinc and acetic acid gives two isomeric *hydroxy*iso*fenchones*, (i) m.p. 114–115°, $[\alpha]_D$ $-31{\cdot}2°$, (ii) m.p. 50–53°, $[\alpha]_D$ $+32{\cdot}4°$, which are presumably stereoisomerides of formula (XVII), since both, on further reduction with sodium amalgam, give d-*epi*iso*fenchone* (XVIII), b.p. 194–196°, $[\alpha]_D$ $+13{\cdot}6°$ (*semicarbazone*, m.p. 219–220°).



(XVI) (XVII) (XVIII)

*iso*Fenchone reacts with bromine to give a *bromo*iso*fenchone*, *d*- and *l*-, m.p. 56–57°, $[\alpha]_D$ $-16{\cdot}4°$ (in alcohol), *dl*-, m.p. 46–47°,‡ which is probably represented by (XIX). With phosphorus pentachloride, the ketone gives a *chlorofenchene*, b.p. 84–87°, which is probably a mixture of isomerides.§

3-*Hydroxymethylene*iso*fenchone* (XX), m.p. 103–104° (*benzoyl* derivative, m.p. 81–82°), has been obtained by Rushentzeva and

---

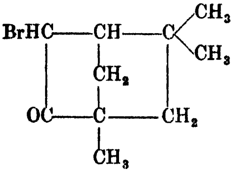
* Komppa and Hasselström, *Annalen*, 1932, **496**, 164.

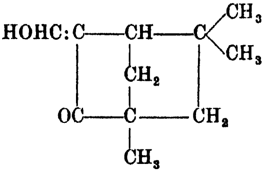
† Alder, Stein and Rickert, *ibid.* 1936, **525**, 221; Rushentzeva and Delektorskaja, *Compt. rend. Acad. Sci. U.R.S.S.* 1940, **29**, 41.

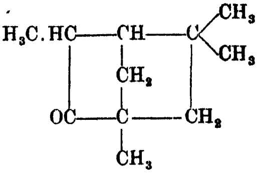
‡ Wallach and Virck, *Annalen*, 1908, **362**, 195.

§ Komppa and Hasselström, *ibid.* 1933, **502**, 272.

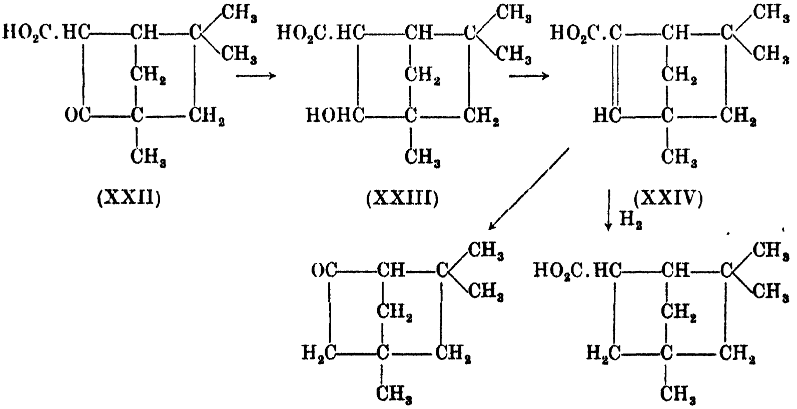
Kedrova* by the action of sodium and amyl formate on the ketone. Similarly, l-3-*methyl*iso*fenchone* (XXI), b.p. 81°/12 mm., $[\alpha]^{18°}_D$ − 19° (*semicarbazone*, m.p. 218°, *oxime*, m.p. 94–95°) has been prepared by reaction of the ketone with sodium and methyl iodide.†


(XIX)


(XX)


(XXI)

On treatment with carbon dioxide, in the presence of sodium, *iso*fenchone gives iso*fenchone-3-carboxylic acid* (XXII), *l*-, m.p. 87–88°, *dl*-, m.p. 114°.‡ Electrolytic reduction of the *dl*-acid gives dl-iso*fenchol-3-carboxylic acid* (XXIII), m.p. 135–137°, converted on dehydration into *δ-fenchene-3-carboxylic acid* (XXIV), m.p. 139–140° (*anhydride*, m.p. 133–135°), the acid chloride of which, on treatment with hydrazine and sodium azide, followed by acid hydrolysis, yields dl-*epi*iso*fenchone* (XVIII), b.p. 195–198° (*oxime*, m.p. 64–65°). On hydrogenation, the acid (XXIV) gives dl-*fenchane-3-carboxylic acid* (XXV), m.p. 103°.



(XXII) (XXIII) (XXIV)

(XVIII) (XXV)

---

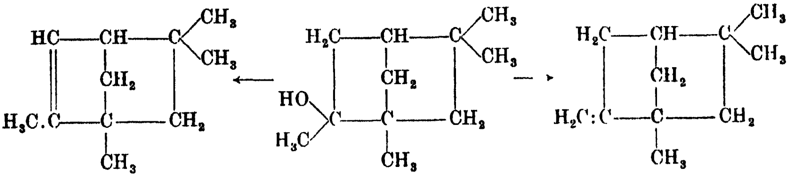
* *Compt. rend. Acad. Sci. U.R.S.S.* 1940, **29**, 95; compare Nyman and Alfthan, *Finska Kemistsamfundet Festskrift-Juhlajulkaisu*, 1891–1941, 1944, p. 291.

† Toivonen and Johansson, *Suomen Kem.* 1942, **15**, Nos. 9–10, B 8.

‡ Nametkin and Rushentzeva, *J. pr. Chem.* 1923 [ii], **106**, 39; *J. Gen. Chem. Russ.* 1937, **7**, 1343; Nyman, *Annalen*, 1939, **537**, 131.

By the action of methyl magnesium iodide on *iso*fenchone, Komppa* has prepared 2-*methyliso**fenchyl alcohol* (XXVI), m.p. 50–51°, b.p. 82°/10 mm. This alcohol on dehydration with potassium hydrogen sulphate gives a mixture of hydrocarbons, which contains 1-*methyl-γ-fenchene* (2-*methyl-δ-fenchene*) (XXVII), b.p. 154–156° (*nitrosochloride*, m.p. 121°), and also 1-*methyl-β-fenchene* (XXVIII), b.p. 163–164°.

It is interesting to note that, unlike *tert.*-methylborneol and *tert.*-methylfenchyl alcohol (compare p. 580), this alcohol apparently does not undergo the Wagner rearrangement on dehydration.


(XXVII) (XXVI) (XVIII)

---

* *Annalen*, 1929, **472**, 179; Komppa and Nyman, *ibid.* 1936, **523**, 87.

INDEX OF AUTHORS

Abakumovskaja, L. N., 278
Achmatowicz, O., 329, 358
Adams, R., 274, 373
Adida, A., 190, 203
Agnew, J. W., 143
Agostinelli, C., 46, 85
Ahrens, H., 428
Akermann, A., 214
Alder, K., 190, 248, 256, 277, 356, 357, 430, 436, 500, 548, 549, 559, 585
Alexandrov, Z., 332
Alfthan, V., 531, 551, 586
Allard, J., 139, 199, 466
Aloy, J., 360, 436
Amann, A., 509
Angeli, A., 315, 416, 441
Angelico, F., 402
Angeloni, L., 492
Angelucci, O., 441
Appel, L., 484
Arbusov, B. A., 70, 134, 141, 142, 199, 200, 293, 447
Arihara, C., 518
Armstrong, H. E., 107, 137, 166, 168, 170, 283, 296, 301, 341, 376, 387, 388, 389, 395, 401, 403, 407, 119, 422, 459, 479, 497
Artamonoff, G. A., [illegible]69
Asahina, Y., 268, 269, 270, 271, 313, 316, 322, 346, 357, 362, 418, 420, 423, 425, 429, 430, 431, 432, 466, 516, 518, 524
Aschan, O., 72, 73, 125, 166, 167, 168, 169, 170, 171, 172, 202, 243, 248, 249, 250, 251, 252, 253, 255, 256, 257, 259, 261, 272, 282, 287, 294, 299, 300, 307, 308, 317, 318, 319, 326, 333, 344, 346, 347, 349, 355, 359, 363, 365, 367, 368, 369, 372, 376, 377, 384, 386, 401, 449, 460, 467, 479, 480, 495, 509, 512, 534, 536, 538, 541, 549, 550, 556, 558, 559, 581, 582
Atterberg, A., 178
Attwell, H. M., 435
Austerweil, G., 165, 198, 203
Autin, E., 214
Auwers, K., 19, 40, 91, 102, 224, 288, 290, 434, 489

Babcock, S. H., 401, 424
Bach, E., 435
Badoche, M., 146, 230
Baer, E., 428, 471
Baeyer, A., 39, 50, 77, 78, 79, 80, 81, 82, 84, 86, 87, 88, 89, 90, 91, 93, 95, 112, 115, 116, 117, 118, 119, 120, 121, 122, 123, 121, 125, 126, 127, 149, 150, 151, 154, 156, 179, 180, 181, 192, 194, 287, 392, 480, 532
Bain, J. P., 205
Bak, B., 274
Balbiano, L., 142, 143, 380, 396, 401, 492, 493, 572
Baly, E. C. C., 385, 434
Banerji, S. K., 545
Barbier, P., 106, 147, 148, 150, 151, 165, 167, 168, 200, 343, 359, 554
Bardhan, J. C., 380, 545, 546, 583, 584
Bardischev, I. I., 435
Barney, A. L., 140
Bartelt, K., 210, 213, 223, 243, 251, 252, 255, 257, 259, 260, 261, 262, 264, 265, 267, 268, 271, 572, 574, 576, 577
Bartlett, P. D., 348
Bateman, L. C., 348
Baubigny, H., 350, 351, 375, 391, 448
Bauer, E., 456, 457
Beauchamp, W. D., 435, 577
Beckmann, E., 353, 365, 383, 391
Beckmann, S., 120, 253, 356, 370, 438, 529, 530, 540, 541, 545, 548, 552, 554, 555, 559
Béhal, A., 437, 440, 444
Bell, R. P., 411
Bellet, E., 273, 326, 343
Berlin, A. A., 297
Bert, L., 177
Berthelot, M., 106, 133, 136, 170, 171, 280, 281, 282, 296, 307, 340, 342, 346, 350, 352, 375, 390, 391
Berton, A. L., 359
Bertram, J., 316, 353, 364, 365, 533, 534, 543, 553, 557, 559, 570, 580
Berzelius, J., 492
Bettelli, C., 203
Bhadhuri, B., 459
Bhagvat, M. B., 469
Bhagvat, W. V., 459
Bhattacharyya, S. C., 270
Biilmann, E. C. S., 274
Billuart, A., 141
Biot, J. B., 106, 374
Birch, A. J., 5, 10, 11, 12, 31
Bishop, A. W., 377, 401, 454, 458, 460
Blaise, E. E., 144, 311, 368, 372, 485

Blanc, G., 311, 368, 371, 372, 378, 444, 484, 485, 494, 504, 506, 507, 508, 513
Blanchet, R., 106, 137, 170, 280, 374
Blanchon, H., 46
Blechschmidt, A., 458
Blumann, A., 138, 139, 194, 195, 215, 217, 218, 219, 220, 233, 234, 235, 237
Blyther, D. K., 186
Bocek, M., 360
Bode, H., 356
Booker, E., 45
Boeseken, J., 165
Bogaheva, 332
Bogert, M. T., 37
Bohny, P., 477
Bone, W. A., 485
Bonino, G. B., 133
Bonnet, G., 104, 197, 207, 212
Bonsdorff, W., 130, 151
Book, L. H., 531, 551
Borgwardt, E., 139
Borrell, C. H. R., 51
Borsche, W., 461
Bose, M. K., 549
Bouchardat, G., 166, 167, 200, 281, 352, 531, 554
Bousset, R., 344
Bouveault, L., 283, 310, 371, 376, 565, 566
Boyle, R., 374
Braucker, R. H., 312
Braun, J. v., 444, 445, 457
Braunschweig, R., 485
Bredt, J., 144, 162, 182, 273, 283, 284, 286, 294, 295, 297, 298, 315, 324, 326, 327, 329, 334, 343, 353, 361, 376, 378, 379, 393, 394, 395, 416, 419, 420, 428, 429, 433, 446, 449, 451, 452, 458, 460, 469, 471, 475, 478, 483, 486, 487, 490, 496, 508, 509, 510, 511, 513, 514, 516, 517, 518, 519, 561, 570, 580
Bredt-Savelsberg, M., 290, 372, 428, 446, 447, 469, 470, 516, 580
Brickner, W., 284, 285, 323, 329, 330, 340, 341, 342, 349
Briellmann, P., 445
Briggs, A. C., 133
Briusova, L. Y., 329, 417, 572
Bromeis, C., 144
Brooks, B. T., 166, 203
Brown, D. C., 21
Brown, J. H., 436, 577
Brühl, J., 281, 283, 376, 377, 402, 405, 409, 448, 449, 452, 453, 456, 458, 459, 460, 462, 485
Brüssoff, L., 290, 580
Brus, O., 167, 198, 199, 201, 202, 363, 386
Brustier, V., 360, 363, 436
Bruylants, G., 33, 34, 47, 170, 376
Bublitz, H., 492
Buchanan, C. B., 385
Bucherer, E., 190, 287, 326
Buchkremer, J., 290, 446, 580
Budnikov, P. P., 178
Budrick, W., 324, 327
Büding, E., 365
Buignet, H., 350
Bund, E., 470, 517
Burcker, E., 494
Burgess, H., 390, 399, 402, 403, 404, 407, 408, 409, 419, 464
Burke, C. E., 509
Burkheiser, K., 451
Burrows, H., 186
Buser, K., 488
Buu-Hoi, N. P., 169, 213
Buxtorf, F., 414

Cahours, A., 350
Cailliot, A., 144
Capitaine, H., 280
Carlson, G. H., 134
Caw, W., 325, 328
Cazeneuve, P., 396, 399, 401, 402, 410, 411, 412
Cella, F., 133
Centnerszwer, M., 385
Chakravarti, R. N., 254, 262, 469
Chambers, A. R., 104, 133
Chandrasena, J. P. C., 439, 504
Chapman, E. M., 381, 382, 427, 469, 482, 486
Charabot, E., 28
Charlton, R. W., 134, 166
Charrier, G., 474
Chautard, I. M., 375
Chautard, J., 106, 355, 479
Chilouet, I., 435, 436, 441
Chisholm, D., 199, 202, 554
Cho, C., 86
Chochrjakova, V. A., 571
Chojn, M., 447
Christ, R. E., 447, 580
Christensen, B. E., 360
Chuchrikova, A. M., 278
Ciamician, G., 392, 570
Claisen, L., 377, 401, 414, 454, 458, 460, 466, 467, 490
Claret, J., 422
Clark, J., 360
Clarke, R. H. L., 85, 90, 402, 466
Claus, A., 395
Cockburn, G. B., 341, 381, 522, 552, 562, 563, 571, 572, 574

Collie, J. N., 283, 376
Collmann, F., 493
Conant, J. B., 134
Conze, C. L., 391, 417, 517
Cooper, K. A., 348
Cormack, W. C., 505, 506, 507
Cornubert, R., 51
Courtot, C., 273, 326
Crossley, A. W., 493, 507, 512
Cusmano, G., 188
Czerny, H., 572

D'Ambrosio, A., 177, 189
Damsky, A., 499
Daniels, J., 246
Darmois, E., 132, 133, 198, 359, 366
Dasgupta, D., 469
Daure, P., 133
Davankov, A. B., 297
Day, A. R., 134, 166
Debierne, A., 383, 479
Delaby, R., 141
Delalande, Z., 374, 395, 443
Delektorskaja, N. M., 585
Delépine, M., 120, 146, 147, 148, 165, 167, 190, 203, 230, 554, 574
Demjanov, N. I., 311
Denaro, A., 170
Derick, C. G., 512
Desch, C. H., 385, 404, 405
Deshapande, S. S., 459
Desalbres, L., 132
Dessaignes, V., 375
Dessauer, H., 312
Detoeuf, A., 310
Deussen, E., 181, 182, 248, 249, 250
Deville, H. St C., 167, 168, 170
Dickison, H. L., 48
Diels, O., 75, 248, 256
Dimroth, O., 464
Dodge, F. D., 283
Doescher, H., 343
Doll, W., 207, 216, 217, 234, 235, 318
Dollfus, F. E., 441
Dormaar, T. M. M., 89
Dorp, W. H. van, 490
Drouven, E., 517
Duden, P., 414, 418, 513, 520
Dulou, R., 134, 139, 166, 199, 223, 224, 300, 369, 569, 580
Dumas, J., 16, 106, 170, 280, 374, 395
Dunn, E. F. M., 385
Dupont, G., 69, 133, 134, 137, 139, 147, 198, 199, 203, 212, 223, 224, 226, 235, 293

Earl, J. C., 10, 180
Easkill, 395
Eastburn, W. J. T., 143
Eckstein, K., 492
Egli, H., 466
Eisenlohr, F., 19, 40, 91, 133, 224, 290
Ekman, F. L., 144
Elder, A. L., 140
Elley, H. W., 386
Elze, F., 210
Emster, K., 158, 170, 171, 276, 307, 308, 332, 333, 338, 347, 348, 349, 355
Engelbrecht, C., 229, 231
Engelmann, F., 342
Engler, C., 137, 139
Enkvist, T., 253, 254, 258, 262
Erich, M. T., 531, 551
Ertschikowski, G., 147, 155, 192
Eschtschenko, A., 329
Eskola, S., 318
Étard, A., 144, 394
Evans, W. C., 353, 466, 468, 492
Eykman, J. F., 512

Faidutti, M., 200, 293
Feldstein, J., 5, 50, 61, 83
Fernandez, O., 149
Ferns, J., 365
Fierz, H. E., 414
Fischer, J. M., 428, 429
Fittig, R., 144, 375, 495, 509
Flatt, W., 414
Flavitsky, F., 166, 168, 169, 170
Fleischner, A., 395
Flückiger, E. A., 105
Fomin, W., 5, 8, 11, 12, 13, 15, 16, 20, 24, 25, 26
Forster, M. O., 185, 186, 190, 309, 313, 325, 387, 388, 389, 399, 400, 405, 407, 410, 414, 416, 418, 428, 432, 434, 435, 436, 437, 441, 446, 455, 457, 461, 463, 464, 465, 467, 469, 471, 472, 474, 475, 476, 477, 478, 519
Frank, E., 556
Frank, W., 435
Frankforter, G. B., 342
Frary, F. C., 342
Fredga, A., 384
Freund, M., 178
Frey, C., 470
Friedel, E., 480
Fromm, E., 16, 28, 32, 214
Frost, H., 75
Fuguitt, R. E., 132, 134, 198
Fujita, Y., 367
Fukushima, 295
Furness, J., 516

Gaind, K. N., 154
Gallas, G., 167, 169
Ganapathi, K., 150, 152, 153, 158, 235
Gandini, A., 104, 274, 326, 328, 342, 441, 576
Ganguly, P. L. N., 393, 483, 583
Gardner, J. A., 281, 283, 301, 303, 311, 381, 433, 495, 532, 552, 562, 563, 571, 572
Garino, M., 177
Garland, C. S., 416
Gascoigne, R. M., 13
Gattefossé, J., 373
Gaudion, G., 134, 293
Gérard, L., 319, 367
Gercke, A., 556
Gerhardt, C., 350, 375, 433
Germuth, F. G., 167
Gibson, C. S., 71, 74, 419, 462, 469
Gilbert, E. C., 360
Gildemeister, E., 105, 130, 147, 148, 206, 207, 209, 227, 228, 231, 280, 349
Gill, J. D., 348
Gillam, A. E., 41, 43, 57, 60, 79, 82, 91, 92, 97
Gilles, W. S., 301
Ginnings, P. A., 436
Ginzberg, A., 111, 138, 172, 173, 176
Glover, W. H., 450, 456
Gobulov, P. G., 280, 363
Godchot, M., 46
Godlewski, J., 166, 306, 333, 527
Goeb, A., 273, 361, 429
Gotzen, A., 287, 307
Goldblatt, L. A., 134, 199
Goldschmidt, H., 402, 437
Goodson, J. A., 435
Goodway, N. F., 76
Gorbunov, T., 78, 81
Gorsline, F. E., 483
Gottlob, K., 135
Grandperrin-Harispe, M., 146, 152
Granger, R., 422
Gratton, G., 246, 370
Gray, T., 142, 144
Griepenkerl, J., 435
Grignard, V., 46, 147, 148, 150, 151, 165, 167, 200, 273, 326, 343, 359, 554
Gripenberg, J., 469
Grosser, B., 394
Gubelmann, I., 386
Guerbet, M., 264, 364, 443, 448
Guha, P. C., 6, 7, 8, 37, 42, 57, 62, 68, 69, 150, 152, 153, 154, 167, 198, 235, 236, 243, 244, 270, 469, 508
Gutt, J., 275

Haarmann, R., 327
Haller, A., 39, 46, 50, 51, 352, 353, 378, 379, 409, 444, 448, 449, 454, 455, 456, 457, 458, 480, 481, 484, 485, 513, 554
Halonen, P., 363
Hammel, O., 309, 319
Hammerich, T., 190, 205
Hantzsch, A., 133, 359, 385, 441
Harazsti, J., 365
Hariharan, K. V., 68
Harmalkar, S., 459
Harries, C., 53, 94, 135, 140, 286, 387, 327
Harris, G., 385
Hartley, W. N., 385
Hartmann, K., 368, 369, 561
Hartridge, A., 385, 433
Hart-Smith, J., 435
Harvey, A. W., 414, 415
Hasselström, T., 31, 232, 261, 267, 271, 278, 370, 423, 526, 542, 573, 585
Hawkins, E., 132, 134, 198, 199, 224, 231, 241
Haworth, W. N., 506
Heaney, J. P., 52
Heilbron, I. M., 144, 309, 327, 328, 359, 366, 385, 569
Hein, F., 424
Heino, E. K., 531, 551
Hello, J., 533, 534, 535, 543, 553, 557, 559, 570, 590
Hempel, C., 166
Henderson, G. G., 5, 11, 20, 21, 25, 30, 32, 142, 143, 144, 173, 176, 199, 202, 273, 276, 294, 309, 325, 327, 328, 330, 359, 366, 385, 554, 569
Henderson, J., 482, 485, 486, 492, 512
Henderson, J. A. R., 385, 569
Henry, T. A., 10
Héritier, A., 210, 213, 214, 224
Hesse, A., 343, 359
Heubaum, U., 435
Heusel, 419, 420
Heymons, A., 445
Hilbing, W., 324, 513, 514
Hintikka, S. V., 245, 246, 253, 286, 288, 311, 331, 368, 370, 371, 538, 555
Hiong-Ki-Wei, 169, 213
Hirschberg, E., 364
Hlasiwetz, H., 282, 375
Hoerlin, J., 499, 500
Hoffmann, F., 105, 280, 349
Hofmann, A. W., 144
Holl, M., 316, 321, 420
Hollemann, A. F., 467
Holmes, H., 467, 474
Holz, W., 315, 329, 416
Homberger, A. W., 511, 581

Hoogewerff, S., 490
Horeau, A., 146
Houben, J., 162, 292, 304, 321, 343, 344, 359, 432, 441, 442, 447, 509, 518, 522
Houzeau, A., 136
Howard, H. A. H., 400, 418, 432
Howard, S. H., 373
Howie, M., 309
Hückel, W., 165, 295, 296, 318, 342, 359, 365, 368, 369, 370, 371, 384, 435, 538, 549, 553, 554, 556, 569, 577, 578
Hugh, W. E., 51, 232
Hughes, E. D., 348
Hultzsch, K., 75
Humphrey, I., 166
Humphrey, L., 203
Hurd, C. D., 447, 580

Ichikawa, N., 210
Igolen, G., 373
Ikeda, T., 360, 367
Iki, T., 390, 431, 432
Immendorf, H., 352
Ingersoll, A. W., 48, 401, 424, 433, 577
Ingold, C. K., 348, 438, 469, 504
Inouye, N., 295
Ipatiev, V. N., 78, 104, 136, 276, 277, 360, 363, 366, 391, 529, 551, 569
Isaac, E., 204
Iselin, M., 460
Ishidate, M., 254, 262, 268, 269, 270, 271, 295, 357, 362, 416, 428, 429, 430, 431, 432, 466, 516, 518, 524
Isshiki, T., 416
Iyer, S. N., 80, 96

Jacev, A. G., 141
Jackson, C. L., 351, 352
Jaggi, A., 480, 492
Jagelki, W., 245, 254, 297, 298, 311, 368, 370, 372
Jahns, E., 33
Jarzev, A., 102, 232
Jatkar, S. K. K., 12, 19, 133, 198, 385, 569
Jenkinson, E. A., 465
Jennings, G., 435, 577
Jensen, K. A., 274
Joffre, M., 66
Johansson, E., 586
Johnson, W. S., 454, 461
Jonas, K. G., 23, 134, 199
Joshel, L. M., 199
Joussen, J., 323
Judd, H. M. D., 455, 461, 465
Jünger, E., 306, 307, 346
Jungfleisch, E., 479, 480

Kaehler, J., 272, 296, 316, 342, 346, 351, 352, 376, 393, 394, 395, 401, 407, 408, 414, 439, 448, 450, 499
Kafuku, K., 210
Kahnemann, 217
Kaku, T., 86
Kalliopin, L. E., 297
Kaluba, H., 359
Kannikov, I. I., 283
Kanonnikov, J., 107, 376, 377
Karrer, P., 428
Kasansky, D. A., 8, 10, 13, 46
Kastler, A., 133
Kawahata, H., 346, 429
Kedrova, N. K., 586
Kekule, A., 106, 107, 168, 170, 282, 395
Keller, C., 400
Kenner, J., 180
Kentish, W. S. K., 462
Kenyon, J., 355, 364, 553, 556
Kerkovius, W., 94
Kermack, W. O., 161
Kerr, C. A., 154, 202
Kerschbaum, M., 148, 149, 233, 234, 237, 504
Kharasch, M. S., 166, 342
Kikina, Z., 274
Kim, C. K., 435, 577
Kindler, H., 538, 549, 553, 554, 569, 577
Kindt, F., 170, 280
Kingzett, C. T., 136
Kipping, F. S., 387, 395, 397, 401, 402, 403, 405, 408, 409, 413, 422, 424, 495, 497, 498, 499
Kirschner, H. G., 295
Kishner, N., 5, 8, 9, 10, 50, 61, 62, 63, 64, 83, 102, 232, 273, 526, 527, 528, 573
Kitchen, L. J., 320
Klages, A., 90, 91, 93, 306, 307, 346
Klami, A., 150, 218, 228, 235, 568
Klever, H. W., 135
Klein, R., 91, 214
Klotz, I. M., 79
Knapp, H., 359, 425
Knicke, L., 469
Knuth, E., 274
Koch, W., 75
Koehler, H., 91, 130, 206, 207, 209, 227, 228, 231
Kohler, V., 147, 148
Koenigs, W., 436, 499, 500
Kohman, T. P., 385
Komppa, G., 120, 150, 218, 228, 235, 245, 246, 253, 254, 259, 261, 263, 278, 279, 286, 295, 301, 302, 311, 331, 335, 336, 356, 368, 370, 371 376, 379, 382, 383, 390, 438, 445, 479, 481, 498, 501, 526, 529, 530, 534, 535, 536, 538 539,

Komppa, G., 540, 541, 542, 544, 545, 548, 551, 552, 555, 559, 568, 573, 585, 587
Komppa, O., 295, 370, 545
Kon, G. A. R., 51, 232
Kondakov, I. L., 11, 12, 15, 16, 19, 21, 26, 35, 78, 81, 107, 172, 309, 342, 533, 542, 555, 559
Kondo, T., 86
Konow, V., 232
Konowalov, M. I., 274, 363, 437, 554, 570
Koolhaas, D. R., 43
Korev, R., 402
Kosegarten, 374
Krafft, O., 144
Kraith, A., 90, 91, 93
Kregten, J. R. N. van, 444
Kremers, R. E., 181
Krestinski, V., 61, 65, 69, 72, 329, 358, 435
Krishnamurthy, S., 6, 8
Kuenzy, F., 580
Küppers, P., 321
Kullhem, M. A., 394
Kumagae, H., 294
Kunz, E., 446, 477
Kuppusami, A., 42
Kurtz, P., 457
Kuvaja, A. M., 228, 521, 560, 580
Kuwata, T., 146, 206, 292, 322
Kyriakides, L. P., 512

Labilliardière, 106
Lafont, J., 163, 167, 200, 281, 352, 554
Lagache, K., 72
Langenbeck, W., 458
Langlois, G., 289, 299, 303, 306, 307, 320
Lankshear, F. R., 513
Lapworth, A., 85, 90, 161, 365, 381, 382, 398, 402, 405, 406, 408, 409, 413, 414, 415, 424, 425, 427, 434, 441, 454, 466, 469, 481, 482, 486, 487, 495, 497, 499, 509, 511
Laurent, A., 374, 400, 489
Lausberg, F., 313, 390, 419
Lavoisier, A., 105, 374
Lawrence, W. T., 144
Leach, F. P., 180, 186, 231
Lebeau, P., 136
Lecomte, J., 169, 213
Lees, F. H., 53, 58, 60, 494
Le Fèvre, R. J. W., 385
Leffler, M. T., 274
Legutke, G., 365
Lemischewski, 331
Lenton, W. H., 482, 495, 509
Lenzlinger, M., 459
Leroide, J., 447, 554
Letts, E. H., 272
Leukart, R., 435
Levallois, F., 565, 566
Levy, P., 509, 510
Levy, S., 16
Lewina, R. J., 8, 63, 103, 136, 338, 529, 551
Lewis, J. R., 499, 500
Lextreit, M. A., 190
Libavius, 374
Liebig, J., 374
Leibl, F., 243, 246, 252, 266, 337, 538
Linstead, R. L., 104, 136
Lipp, A., 102, 103, 125, 158, 162, 196, 199, 246, 267, 276, 277, 287, 292, 299, 306, 307, 311, 312, 313, 316, 321, 334, 335, 337, 354, 355, 359, 368, 390, 391, 417, 419, 420, 425, 444, 445, 489, 517, 569
Lipschitz, W., 365
Lischke, W., 28
List, C., 106
Littlebury, W. O., 359, 360, 364, 366
Littleton, L. R., 504
Liveroski, A., 65
Locquin, R., 392
Lohr, H., 45
Lombard, R., 137
Lorentz, G., 181
Lossen, W., 515
Loudon, J. D., 385, 389
Louvrier, J., 457
Lowry, T. M., 385, 387, 388, 389, 390, 396, 397, 399, 400, 401, 402, 403, 404, 405, 407, 410, 411, 412, 413, 419, 420, 422, 450, 464, 497
Lubovcova, K. B., 571
Lutschinin, E., 309, 533, 555
Lynn, E. V., 179, 180

McAlevy, A., 493
McAlpine, I. M. I., 327, 359, 365
Macintyre, A. E., 414, 513
Mackonkey, C. A. H., 464
Magnus-Levy, A., 429
Magson, E. H., 420, 422, 424
Mahla, F., 441, 443, 444, 480, 576
Maihle, H., 102, 134
Mair, J. A., 330
Malaguti, 374
Malberg, W., 65
Malevskaya, S., 72
Malmgren, S. M., 402, 449, 458, 462, 464
Manasse, O., 377, 414, 427, 429, 466, 467, 468, 469, 490
Manske, R. H. F., 441
Manz, G., 444
Margueron, 137

Markownikov, W., 390
Marsden, E. G., 385, 434
Marsh, J. E., 281, 283, 301, 303, 306, 311, 385, 401, 403, 409, 433, 495, 563, 573
Marsh, J. K., 173, 196
Martin, H., 418
Martine, C., 46
Masumoto, B., 360
Mathieu, J. P., 385
Matthews, 401
Maull, C., 512
May, P., 334
Mayekawa, T., 316, 420, 423
Mazza, F. P., 470
Meerwein, H., 158, 159, 163, 170, 171, 172, 246, 272, 276, 303, 304, 307, 308, 309, 319, 323, 332, 333, 338, 347, 348, 349, 350, 355, 367, 433, 434
Meesen, K., 457
Meisenheimer, J., 384, 472
Menke, A. E., 351, 352
Menon, K. N., 55, 68, 75, 81, 85
Merling, E., 441
Mettegang, M., 312
Meyer, I., 429
Meyer, V., 375
Meyn, O., 446
Michaelis, K. O. A., 104, 136
Michailov, B. M., 70, 141
Mickelthwait, F. M. G., 448, 465
Miettinen, J. K., 384
Migliardi, C., 470
Milas, N. A., 493
Miller, A. K., 376, 395, 554
Minguin, J., 359, 448, 449, 453, 454, 455, 456, 457, 458
Mirasierra, G. de, 149
Mitchell, E. C., 133
Mitter, P. C., 3
Miyake, K., 394, 438
Mohler, H., 45
Mohunta, L. M., 243
Moitessier, A., 494
Momose, T., 268, 269, 270, 466, 524
Monheim, J., 395, 469
Montalbano, G., 402
Montanes, J. M., 167, 169
Montfort, F., 163, 349
Montgolfier, E., 351, 352, 353, 448
Montgolfier, M. J., 272, 401
Moore, W. R., 448
Morani, V., 384
Morgan, G. T., 448
Mosher, W. A., 165
Mousseron, M. S., 422
Moycho, S., 297, 317, 331, 333, 355, 370, 371
Müller, F., 428, 467
Müller, O., 243, 245, 249, 250, 264, 268
Muir, M. M. P., 33
Mukherji, D., 545, 546, 583, 584
Muliar, P. A., 360
Murayama, Y., 190, 518, 520
Muthanna, M. S., 37, 57

Nägeli, E., 377, 434, 437
Nakatsuchi, A., 178
Nakazawa, K., 429
Nametkin, S., 102, 141, 162, 232, 274, 278, 290, 291, 292, 314, 315, 329, 332, 339, 371, 447, 522, 526, 528, 530, 548, 566, 571, 580
Nath, B., 7
Naudin, E., 167, 176
Naves, Y. R., 57, 75, 95
Neave, G. B., 360, 366, 555
Nelson, E. K., 21, 191
Neresheimer, H., 140
Neuberg, C., 364
Neudel, F., 435
Neumann, E., 318, 543
Neunhoeffer, O., 556
Nevell, T. P., 161, 349
Newman, S. H., 185, 186
Nickell, L. F., 504
Niemann, J., 461
Nikitin, V. M., 134
Noyes, W. A., 435, 436, 483, 490, 491, 503, 504, 505, 509, 511, 512
Nyman, G. A., 246, 253, 259, 263, 356, 370, 521, 536, 538, 539, 541, 542, 551, 560, 580, 586, 587

Oakberg, F. S., 373
Oberright, E. A., 140
Oddo, G., 402, 448, 466
Oeckinghaus, E., 391, 417, 517
Östling, G. J., 8, 26, 44, 45, 91, 133, 194, 290, 338, 385, 551
Olberg, R. C., 104
Onischtschenko, A. S., 250
Oppenheim, A., 106, 107, 168, 170, 281
Oppermann, C., 280
Orita, T., 86
Ost, W., 231
Otsuka, K., 190
Otto, A., 109
Owen, J., 65, 68, 69, 74

Padmanabhan, R., 12, 19, 133, 198, 385, 569
Paget, H., 10
Paillard, H., 167

Palkin, S., 134, 199
Palmén, J., 244, 261, 262, 286, 287, 460
Panicker, P. M. B., 65
Paolini, V., 24, 25, 30, 44
Papazian, G., 75
Pariselle, H., 133, 198, 202, 306
Pasquarelli, A., 422
Passerini, M., 344, 441
Patterson, T. S., 365, 385
Paul, M., 69
Peignier, P., 355, 359, 365, 391
Peligot, E., 395
Pelouze, J., 350, 374
Penfold, A. R., 16, 73, 95, 97, 210, 212
Perkin, sen., W. H., 400
Perkin, jun., W. H., 65, 78, 115, 122, 124, 125, 126, 147, 149, 153, 198, 326, 343, 376, 379, 382, 393, 475, 493, 494, 500, 501, 504, 505, 506, 507, 513, 514, 516
Perrichet, J., 385
Pesci, L., 203
Peyresblauques, G., 199
Pfaff, E., 281, 435
Pfankuch, E., 292, 304, 343, 344, 432, 441, 442, 447, 522
Phillips, E. D., 56
Phillips, E. F., 503
Pickard, R. H., 359, 360, 364, 366, 515
Pickles, S. S., 10
Picon, M., 136
Pietrzok, H., 342
Pigulewski, G., 465
Pillay, P. P., 69, 70
Pines, H., 104, 272, 363, 529, 551
Pinten, P., 518
Plein, E. M., 384
Poe, C. F., 384
Pöckell, I., 348
Poggi, A. R., 422
Pollock, E. F., 273, 276, 327
Ponndorf, W., 215, 216
Ponzio, G., 474
Pope, W. J., 137, 387, 400, 401, 402, 405, 408, 419, 422, 424, 434, 435, 459, 462
Pospischill, K. T., 243
Pott, R., 395
Potter, R. S., 483, 503
Power, F. B., 53, 60
Prasad, S., 385
Preis, K., 170
Presting, W., 5, 20, 79, 80
Prileschaev, W., 141, 200
Priston, H. E. M., 355, 364, 553, 556
Pritzkov, W., 414, 520
Prokoptschuk, W., 200
Prostakov, N. S., 513
Puliti, J., 396, 449
Purvis, J. E., 569

Quaedvlieg, M., 321
Qudrat-i-Khuda, 486
Qvist, W., 527, 534, 538, 539, 548, 558, 559

Rabak, F., 28, 64
Rabourdin, S. M., 144
Ramage, G. R., 56, 210, 212
Ranganathan, S. K., 57, 243, 244, 583
Ranta, S., 39
Rao, B. S., 65
Rao, K. A. N., 472
Rao, P. L. N., 148, 153, 236
Rast, K., 385
Rau, M. G., 13, 16, 69, 76, 137
Ray, J. N., 243
Rayman, B., 170
Read, J., 17, 24, 25, 30, 39, 45, 46, 48, 49, 50, 96, 360, 422, 435, 459, 462
Rebora, G., 30
Reddelien, G., 446
Regler, H., 424
Rehorst, K., 190
Reinartz, F., 287, 307, 457
Reinartz, R., 429, 570
Reisman, J., 167
Renouf, N., 507, 512
Renwick, F. F., 301
Revis, C., 405
Rewald, A., 419
Reychler, A., 281, 305, 307, 346, 388, 389, 419, 420
Reynolds, W. B., 166
Riban, J., 170, 171, 281, 296, 301, 307, 346
Richter, F., 5, 20, 79, 80, 198
Rickert, H. F., 559, 585
Ridgion, J. M., 393, 466, 468
Rimini, E., 260, 261, 436, 441, 574, 576
Ritter, J. J., 141, 166, 293, 446
Rivière, C., 343, 344
Robertson, A., 11, 20, 25, 30, 32
Robertson, A. R., 5
Robertson, J. M., 21
Robertson, W., 410, 413
Robertson, W. A., 373
Robinson, H. H., 64, 65
Robinson, R., 2, 159, 161, 365
Rochusson, F., 395, 419, 420, 469
Rohrmann, W., 254, 501
Roll, L. J., 132, 134
Roschier, R. H., 279, 331, 371, 530, 535, 538, 539, 540, 542, 544, 545
Rosenberg, M., 379
Roser, W., 144, 394
Roth, W. A., 8, 19, 26, 45, 91, 133, 290, 338, 385

Roy, A. N., 69, 167
Royer, R., 169, 213
Royère, W. de la, 407
Royle, F. A., 487
Rudakoff, G. A., 69, 135
Rule, H. G., 104, 133
Rummelsberg, A. L., 104
Rumscheidt, C., 447
Rupe, H., 53, 94, 210, 213, 214, 224, 269, 385, 414, 418, 428, 445, 458, 459, 460, 462, 466, 467, 470, 477, 480, 488, 490, 491, 492, 512, 580
Rushcntzeva, A. K., 585, 586
Russell, K. L., 141
Rutovski, B. N., 191, 205, 360
Ruzicka, L., 43, 75, 128, 130, 158, 178, 184, 185, 220, 228, 232, 243, 246, 252, 265, 266, 325, 337, 446, 449, 538, 566, 567, 576, 580
Rydon, H. N., 56

Sabatier, P., 100, 102, 134, 275, 276, 293
Sahashi, Y., 429, 431
Salas de, E., 161, 348
Salmon-Legagneur, F., 481, 484, 495, 516
Samuel, E., 468, 469
Sandelin, A. E., 582
Sandkuhl, H., 324, 449, 451
Sankaran, D. K., 62, 68
Sano, T., 254, 262, 316, 322, 357, 420, 423, 432
Santos e Silva, J. de, 401, 449
Saprikin, S., 172
Sauer, H., 312
Savelsberg, M., 446
Savich, T. R., 134
Seal, C., 135
Scarlato, G., 170
Schaef, E., 169
Schavrigin, A. I., 290, 292, 447, 513
Schenk, D., 389, 419
Schiff, H., 138
Schiff, R., 396, 401, 402, 410, 414, 416, 449
Schiller, v. H., 65, 68, 71, 73, 75
Schimmel & Co., 23, 227, 251, 253, 257, 260, 552, 560, 561
Schindelmeiser, J., 81, 342, 555
Schlaepfar, M., 416
Schlochoff, P., 53
Schmidt, H., 21, 31, 46, 65, 74, 103, 104, 144, 177, 185, 199, 207, 209, 210, 212, 215, 216, 221, 222, 223, 224, 226, 230, 231, 240, 242, 297, 542, 553, 554, 559, 569, 570
Schmidt, R., 437
Schmiedeberg, O., 429
Schmitz, E., 360
Schneider, I., 318
Schnell, H., 489
Schönbein, C. F., 106, 136
Scholl, C., 517
Schossberger, E., 16
Schotz, S., 450, 451
Schreder, J., 144
Schrotter, H., 361, 394
Schryver, S. B., 110, 144, 511
Schulz, L., 207, 216, 217, 234, 235, 553, 569, 570
Schumann, L., 517
Schumann, W., 169
Schumm, P., 139, 215, 216, 219, 235
Schwalbe, A., 319, 365
Schwanert, H., 395
Schwenk, E., 139
Sebe, Y., 210
Seitz, R., 140
Sell, E., 106, 137, 170, 280, 374
Semmler, F. W., 5, 15, 16, 17, 21, 22, 23, 25, 26, 28, 31, 33, 34, 35, 36, 37, 39, 40, 46, 47, 50, 51, 53, 54, 55, 57, 60, 61, 65, 68, 71, 73, 75, 77, 83, 112, 118, 119, 120, 121, 122, 123, 126, 134, 148, 169, 192, 210, 211, 213, 223, 224, 243, 248, 251, 252, 255, 257, 259, 260, 261, 262, 264, 265, 266, 267, 268, 271, 272, 275, 276, 286, 287, 295, 303, 306, 307, 309, 316, 333, 341, 347, 349, 354, 355, 359, 368, 371, 372, 438, 563, 566, 572, 574, 576, 577, 580, 581
Sen, D. C., 446
Senderens, J. B., 100, 102, 275, 276
Sen-Gupta, S. C., 258
Serini, A., 309, 319
Servant, R., 133, 198
Seyler, H., 5, 36
Sharefkin, J. G., 166
Shelberg, W. E., 454, 461
Shenstone, W. A., 178, 179
Shepheard, F. G., 206, 232
Sherred, J. A., 411
Shilov, E. A., 178
Shocket, D., 104
Short, A. G., 17, 24, 25, 30, 39, 45, 46, 48, 49, 50, 96
Short, W. F., 545
Shotton, J. A., 421
Shriner, R. L., 421
Shukla, P. P., 428
Silber, P., 392, 570
Simonsen, J. L., 10, 12, 14, 16, 36, 55, 56, 65, 68, 69, 70, 71, 72, 73, 74, 75, 80, 81, 85, 95, 96, 97, 117, 144, 147,

Simonsen, J. L., 149, 153, 156, 198, 210, 212, 246, 370, 373, 393, 462, 466, 468, 469, 499, 500
Sinclair, W., 377, 401, 454, 458, 460
Singh, B. K., 385, 459, 478
Sivkoff, A. I., 291
Skita, A., 102
Skworzov, W., 11, 12, 15, 16, 19, 21, 26
Slawinski, K., 146, 172, 173, 194, 309
Smirnov, W. A., 166
Smith, C., 133
Smith, D. F., 134
Smith, E., 144
Smythe, J. A., 206
Snitter, P., 246
Soden, H., 264
Solodki, F., 61, 69
Sonnenfeld, E., 139, 235
Souberain, E., 280
Souza, M. de, 489
Spath, A., 169
Spencer, C. C., 140
Spinner, H., 475, 478, 519
Spitzer, F. V., 272, 296, 307, 316, 322, 351, 352, 401, 407, 408, 414, 433, 439, 448, 450
Splittgerber, I., 466, 490, 491
Sprankling, C. H. T., 485
Stallcup, W. O., 132, 198, 199, 224, 231, 241
Staudinger, H., 135, 450, 451
Stschukarev, 168
Steele, V., 397, 403, 410, 411
Stein, G., 190, 277, 356, 357, 430, 436, 548, 549, 559, 585
Steinbrink, H., 196
Steindorff, A., 461
Steinkopf, W., 178
Stephan, K., 190, 205
Stewart, A. W., 385, 434
Stillman, J. M., 52
Stockdale, R., 281
Stokes, J. A., 190
Stoll, M., 265
Stratford, R., 165
Struthers, J. E. M., 409
Stüsser, R., 267, 389, 419, 423
Stutzinger, G., 292
Sua, E., 167
Subramanian, V., 152, 153, 508
Sudborough, J. J., 485
Sugiura, E., 33
Susuki, K., 137, 139
Sutherland, H. S., 421
Sutherland, M. M. J., 142, 294
Svanberg, L., 144
Swaminathan, R., 583
Swan, G., 134
Swarts, F., 400, 405, 407
Sykes, H. I., 140

Tafel, J., 360, 435, 492
Takashima, N., 428
Takeuchi, K., 417, 430
Tanaka, S., 520
Tappe, W., 365, 370
Tardy, E., 531, 580
Taveau, R. de, 483, 509
Taylor, G., 133
Taylor, T. W. J., 472
Tempa, P., 167
Theilacker, W., 384, 472
Thiel, W., 119, 438
Thiele, J., 515
Thielke, R. C., 133, 179, 341
Thomas, S. L. S., 104, 136
Thommen, W., 467
Thomson, D., 36, 51
Thorpe, J. F., 65, 78, 122, 124, 126, 376, 379, 382, 393, 504
Thurber, F. H., 132, 133, 134, 179, 341
Tideman, C. G., 385
Tiemann, F. W., 34, 36, 37, 38, 48, 77, 112, 118, 119, 120, 121, 122, 123, 126, 147, 148, 149, 192, 284, 376, 377, 414, 418, 437, 438, 439, 440, 441, 443, 444, 480, 504, 509, 561, 576
Tigges, H., 509
Tilden, W. A., 106, 107, 130, 134, 166, 168, 170, 178, 179, 181, 186, 190, 206, 232, 296, 301, 479
Timtschenko, 554
Tingle, J. B., 454
Tischenko, V. E., 135
Todenhöfer, K., 57, 58, 59, 552, 554, 559
Toivonen, N. J., 263, 357, 362, 363, 390, 529, 531, 536, 551, 560, 584, 586
Tollens, B., 375
Tomi, W., 269
Trebler, H., 128, 130, 184, 185, 220, 228, 232
Treibs, W., 21, 31, 46, 104, 144, 222, 231, 237, 242, 287, 542
Triem, G., 458
Tschugaev, L. A., 5, 8, 10, 11, 12, 13, 15, 16, 20, 24, 25, 26, 49, 130, 209, 323, 324, 325, 327, 359, 364, 385, 465, 533, 556
Tukamoto, T., 362, 418, 423
Tutin, F., 53, 54, 55, 57, 58, 60

Urbain, E., 135
Urban, L. C., 181
Urry, W. H., 342

Vaugin, M., 344
Vavon, G., 102, 199, 277, 343, 344, 355, 357, 359, 365, 391, 435, 436, 441
Vène, J., 393, 466, 481, 484
Verschuk, V., 141
Vignano, A., 414, 418, 470
Villiger, V., 192, 194, 287, 392, 480
Vinogradova, I. V., 199, 205
Vitte, G., 181
Vivek, P., 534, 542, 557, 584, 585
Vixseboxse, H., 464
Vlases, G., 293
Vorster, J., 171, 309, 319

Wagner, G., 35, 78, 109, 110, 111, 112, 118, 127, 128, 138, 145, 146, 147, 156, 172, 173, 176, 192, 194, 201, 283, 284, 285, 286, 287, 289, 297, 299, 322, 328, 330, 331, 333, 340, 341, 342, 349, 354, 359, 368, 371, 513, 522
Walbaum, H., 316, 364, 365
Walker, J., 480, 482, 485, 486, 488, 492, 502, 505, 506, 507, 512
Wallach, O., 12, 14, 15, 17, 19, 20, 21, 22, 23, 26, 28, 30, 32, 33, 34, 35, 36, 37, 39, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 67, 88, 89, 90, 91, 93, 94, 103, 105, 107, 108, 109, 110, 111, 116, 130, 133, 137, 143, 148, 166, 167, 168, 169, 170, 178, 179, 180, 181, 182, 183, 184, 185, 194, 195, 196, 198, 201, 202, 203, 204, 206, 221, 227, 229, 230, 231, 232, 237, 240, 281, 282, 283, 305, 316, 342, 349, 352, 363, 435, 446, 461, 493, 531, 532, 533, 534, 535, 538, 539, 542, 543, 552, 554, 555, 557, 558, 560, 561, 562, 563, 565, 569, 570, 572, 573, 574, 576, 577, 578, 579, 580, 581, 582, 584, 585
Walter, P., 499
Watanabe, M., 438
Weaver, W. I., 140
Wechsler, E., 402, 466
Wedekind, E., 267, 389, 419, 423
Wegler, R., 435
Weidner, H., 318
Weigand, W., 287, 326
Weitzenböck, R., 394
Werner, J., 37
West, T. F., 41, 43, 57, 60, 76, 79, 82, 91, 92
Weyl, W., 375, 390
Whitby, G. S., 448
Widmann, O., 106
Wienhaus, H., 57, 58, 59, 65, 74, 139, 215, 216, 235, 446, 570, 579
Wiggers, A., 166
Willfroth, F., 343
Williams, W. C., 144
Willstatter, R., 139, 235
Wilson, C. L., 161, 348
Windemuth, E., 357, 500
Winkelmann, E., 169
Winzer, H., 487, 488
Withers, J. C., 469
Wolf, E., 312
Wolff, L., 526, 527, 528, 573
Wolff, W., 5, 20, 79, 80, 102, 158, 273
Wolowski, H., 553, 554, 569, 577, 578
Wood, J. K., 480, 488
Woodward, R. O., 385
Wootton, W. C., 491
Woringer, L., 495, 509
Wornast, W., 190, 492
Wortmann, W., 272, 303, 304, 338, 433, 434
Wreden, F., 376, 480, 495, 512

Yamaguti, K., 313
Yates, J., 494

Zaar, B., 211, 223, 224
Zabrodin, A. S., 314, 315, 339
Zacharewicz, W., 140, 199, 212, 223, 224, 226, 235
Zanke, W., 570
Zaugg, H. E. I., 573
Zaunbrecher, K., 469
Zavadovsky, A., 61, 63, 64
Zeitschel, O., 138, 139, 167, 215, 217, 218, 219, 220, 233, 234, 235, 237, 552
Zelinski, N. D., 8, 10, 13, 46, 63, 102, 103, 136, 275, 276, 338, 343, 446, 449, 528, 529, 551, 579
Ziekendraht, C., 488
Ziegler, K., 169
Zienkowski, F., 297, 317, 331, 333, 355, 370, 371
Zimmerli, A., 477

INDEX OF SUBJECTS

(The principal references are shown in Clarendon type)

Abies Sibirica, oil from, 280
2-Acetoxyapocamphanealdehyde, 312
4-Acetylborneol, 447
ω-Acetylcamphene, 321
3-Acetylcamphor, 455, 462
3-Acetyl*cyclo*pentanecarboxylic acid, 243, 244
Allylborneol, 447
3-Aminoborneol, 414
tert.-Amino*iso*bornylane, 529
ω-Amino*iso*camphane, 312
α-Aminocamphene, 314
1-Aminocamphene, 313
3-Aminocamphonanic acid, 490, 509
α′-Aminocamphor, 414
*iso*Aminocamphor, *see* Dihydro-β-campholenoiminolactone
4-Aminocamphor, 433, 524
α′-Aminocamphoroxime, 414
Aminodihydro-α-campholytic acid, 491, 503
2-Aminoepicamphor, 520
tert.-Amino-β-fenchane, 531
Aminonopinone, acetyl derivative of, 184
Aminopinene, 204
ω-Aminotricyclene, 335
Andropogon Jwarancusa Jones, oil from, 73
Anhydrofenchocarboxylic acid, 578
Anilomethylenecamphor, 459
Apoborneol, *see* α-Fenchocamphorol
π-Apoborneol-7-carboxylic acid, 269, 357
Apobornyl chloride, 245, 370, 542
Apobornylene, **331**, 370, 542
Apocamphenecarbinol, 270
Apocamphenecarboxylic acid, 269
π-Apocamphor-π-carboxylic acid (*see also iso*Ketopinic acid), 267
Apocamphoric acid, 301, 331, 341, 390, 528, 549, 562
— acid, synthesis of, 301 539
Apocamphoric anhydride, 302
Apocyclene, 246, 331, 332, 370, 372, 542
Apofenchene, 565
— nitrosochloride, 565
Apo*iso*fenchene, 542
Apofenchocamphoric acid, 279, 332, 544, 547
— acid, synthesis of, 545
Apofenchyl chloride, 565
Aposantenol, 264
Aposantenone, 264
Artemisia absinthium L., oil from, 33
Artemisia tridentata, oil from, 373
"Artificial camphor", 170, 280, 340
Asarum Sieboldi var. *seoulensis* Nakai, oil from, 86

Balbiano's acid, 380
ω-Benzoylborneol, 321
ω-Benzoylcamphene, 322
α-Benzoylcamphor, 457, 463–5
ω-Benzoylcamphor, 321
O-Benzoylcamphor-3-carboxylic acid, methyl ester, 453
Benzylcamphor, 464
Benzylidenecampholic acid, 458
α-Benzylidenecamphor, 457, 464
α-Benzylidenecamphoroxime, 457
Benzylidene-eucarvone, 88, 94
Benzylidenesantenone, 261
Benzylidenethujone, 51
Blumea balsamifera, oil from, 349, 373
Borneene, 281, 351
Borneocamphene, 281
Borneocamphor, 349, 373
Borneol, 156, 199, 203, 328, **349**
— , action of halogen acids on, 363
— , action of halogens on, 363
— , action of potassium hydroxide on, 364
— , bornoxyacetate, 360
— , 2-chlorocymene-5-sulphonate, 320
— , constitution of, 353–5
— , dehydration of, 363
— , 3:5-dinitrobenzoate, 358
— , distinction from *iso*borneol and camphene, 359
— , *p*-nitrobenzoate, 359, 366
— , oxidation of, 360–3, 466
— , physical properties of, 359
— , picrate, 190, 203

Borneol, purification of, 360
— , reduction of, 275, 360
— , separation from *iso*borneol, 353, 364
— , stereochemistry of, 355, 362
— , synthesis of, 358
— , tautomerism with *iso*borneol and camphene hydrate, 355
— , *p*-toluenesulphonate, 364
— , urethanes, 364
*iso*Borneol (*see also* Borneol), **365**, 391
— , derivatives of, *see* Borneol
— , oxidation of, 366
— , physical constants of, 366
— , reduction of, 354, 366
π-Borneol, *see* Dihydroteresantalol
ω-Borneol, 432
Borneol-3-carboxylic acid, 324, 451, 521
Borneol-4-carboxylic acid, 344, 447, 524
Borneol-π-sulphonic acid, 423
Borneol-ω-sulphonic acid, 420
Bornoxyacetic acid, 360
Bornylamine, 435, 441
*neo*Bornylamine, 435, 441
*iso*Bornylane, **528**, 541, 551
— , action of nitric acid on, 529
Bornyl bromide, 169, 172, 349
*iso*Bornyl bromide, 309, 349
Bornyl chloride, 156, 272, 281, **340**
— chloride, action of magnesium on, 326, 343
— chloride, action of nitric acid on, 302, 341
— chloride, conversion into camphene and *iso*borneol, 342
— chloride, equilibrium with *iso*bornyl chloride and camphene hydrochloride, 171, 319, 323, 347
— chloride, oxidation of, 341, 381
— chloride, reduction of, 342
*iso*Bornyl chloride, 307, **340**
— chloride, conversion into camphene and *iso*borneol, 347
— chloride, equilibrium with bornyl chloride and camphene hydrochloride, 171, 319, 323, 347
— chloride, reduction of, 347
Bornyl dibromide, 168, 333
Bornyl dichloride, 167, 272
Bornyldimethylamine, 325
Bornyl disulphide, 365
Bornylene, 285, **322**, 518
— , action of chlorine on, 328
— , action of hydrogen halides on, 329
Bornylene, action of hypochlorous acid on, 330
— chlorohydrin, 309, 330
— , constitution of, 326
— , hydration of, 330, 513
— hydrohalides, 329
— nitrosite, 327
— , oxidation of, 326, 327, 328
— , physical constants of, 327
— , reduction of, 273, 274, 327
*iso*Bornylene, *see iso*Tricyclene
β-Bornylene, *see iso*Tricyclene
Bornylene-2-carboxylic acid, 343, 521
Bornylene-3-carboxylic acid, 324, 451 460
— acid, conversion into epicamphor, 514, 521
Bornylene-6-carboxylic acid, 344
Bornylene-3-*iso*cyanate, 515
Bornylene-2-hydroxamic acid, 521
Bornylene-3-hydroxamic acid, 515, 521
Bornylenol, 314
Bornylglucoside, 365
Bornyl iodide, 172, 272, 285, 323, 349
*iso*Bornyl iodide, 309, 349
*iso*Bornyl methyl ether, 367
*iso*Bornylol, 529
*iso*Bornylone, 531
Bornyltrimethylammonium iodide, 325
Boswellia Carterii, oil from, 214
Boswellia serrata Roxb., oil from, 10
α′-Bromo-α-benzylcamphor, 456
2-Bromocamphane-3-carboxylic acid, 325
3-Bromocamphane-3-carboxylic acid, 514
ω-Bromocamphene, 287, 305, 321
6-Bromocamphene, 337
Bromocamphenic acid, 299
Bromocamphenilanic acid, 298
α-Bromocampholenic acid, 408
Bromocampholic acid, 444
α-Bromocampholide, 406
Bromocamphonanic acid, 509
α-Bromocamphor, 400, 407, 448, 462, 466
— , mutarotation of, 403
α′-Bromocamphor, 403
π-Bromocamphor, 405, 409
— , conversion into π-hydroxycamphor, 430
ω-Bromocamphor, 387, 404, 407
— , action of ammonia on, 418
5-Bromocamphor, 417
α-Bromocamphor-α′-carboxylic acid, 401, 449

Bromocamphorenic acid, 406
β-Bromocamphoric acid, 390
π-Bromocamphoric acid, 409, 497
ω-Bromocamphoric acid, 390, 497
4-Bromocamphoric acid, 496
α-Bromocamphoric anhydride, 495, 509
π-Bromocamphoric anhydride, 499
π-Bromocamphoroxime, 405
ω-Bromocamphoroxime, 404
ω-Bromocamphorquinone, 404
α-Bromocamphor-π-sulphonamide, 424
ω-Bromocamphor-α-sulphonamide, 404
ω-Bromocamphor-α-sulphonic acid, 404
α-Bromocamphor-π-sulphonic acid, 402, 424
α-Bromocamphor-ω-sulphonic acid, 422
α-Bromocamphor-π-sulphonyl bromide, 408
α-Bromocamphor-ω-sulphonyl bromide, 407
ω-Bromocamphor-α-sulphonyl chloride, 404
π-Bromocamphor-π-sulphoxide, 267, 423
π-Bromocamphoryloxime, 413
ω-Bromocamphoryloxime, 413
α-Bromo-α′-cyanocamphor, 455
*iso*Bromodihydro-β-camphylic acid, 500, 501
α-Bromodihydro*iso*lauronolic acid, 507
β-Bromodihydro*iso*lauronolic acid, 507
2-Bromoepicamphor, 519
2-Bromoepicamphor-2-carboxylic acid, 519, 520
α-Bromo*iso*fenchocamphoric acid, 582
Bromofenchone, 572
Bromo*iso*fenchone, 585
α-Bromo-α′-formylcamphor, 460
Bromo*iso*lauronolic acid, *see* *iso*Dibromodihydro-β-camphylic acid
8-Bromo-*m*-menthane, 63
α′-Bromo-α-methylcamphor, 456
2-Bromo-2-nitrocamphane, 313, 387, 436
α-Bromo-α′-nitrocamphor, 401, 404, 405, 410
α′Bromo-α-nitrocamphor, 402
π-Bromo-α′-nitrocamphor, 410, 413
ω-Bromo-α′-nitrocamphor, 413
2-Bromopinane, 104
Bromopinic acid, 115, 151
Bromotetrahydrocumic acid, 193
2-Bromo-1:1:2-trimethyl*cyclo*pentane-5-carboxylic acid, 504

Camphanamide, 482
Camphane, **272**, 327, 338
— , action of chlorine on, 274
— , nitro-derivatives of, 274, 328
*iso*Camphane, **275**, 338, 391
— , nitro-derivatives of, 278
— , oxidation of, 277
Camphane-2-aldehyde, 343
Camphane-2-carbinol, 344
Camphane-2-carboxylic acid, 343, 520
Camphane-3-carboxylic acid, 325, 451, 513
*iso*Camphane-1-carboxylic acid, 344
*iso*Camphane-4-carboxylic acid, 346
Camphanic acid, 380, 495, 509
— acid, methyl ester, 496
π-Camphanic acid, 498
ω-Camphanic acid, 497
Camphenanic acid, 294, 297, 328
*iso*Camphenanic acid, 294, 328
Camphene, 106, **280**, 363, 365, 435
— , action of acetyl chloride on, 321
— , action of benzoyl chloride on, 321
— , action of ethyl diazoacetate on, 287
— , action of halogen acids on, 307
— , action of halogens on, 303
— , action of hydrazoic acid on, 322
— , action of hypochlorous acid on, 309
— , action of nitric acid on, 300, 310
— , action of trioxymethylene on, 320
— chlorohydrin, 309
— , constitution of, 282–9
— , conversion into *iso*borneol, 159, 316, 365
— , direct conversion of pinene into, 135, 290
— , formation from *iso*borneol, 156, 158, 290
— glycol, 283, 297
— hydrate, 308, 315, 317
— hydrate, dehydration of, 318
— hydrate, tautomerism of, 319, 320
— , hydration of, 315, 319, 353, 365
— hydrobromide, 309
— hydrochloride, 308
— hydrochloride, equilibrium with bornyl and *iso*bornyl chlorides, 171, 319, 323, 347
— methyl ether, 319
— nitrate, 310
— nitronitrosite, 311, 313
— nitrosite, 277, 311, 312

Camphene, oxidation of, 283, 293–303
— oxide, 293
— , physical constants of, 289
— , racemisation of, 290–2
— , reduction of, 275, 276, 293
— selenide, 303
— , synthesis of, 289
Camphene-camphoric acid, *see* Camphenic acid
Camphene-ω-carboxylic acid, 307, 320
Camphene-1-carboxylic acid, 344, 523
— acid, amide, 442
Camphene-4-carboxylic acid, 346
— acid, amide, 442
Camphene-7-carboxylic acid, 452
Camphenehydrato-4-carboxylo-π-sulpholactone, 346
Camphenehydrato-π-sulpholactone, 317
Camphenic acid, 284, 296, 299, 412
Camphenilanaldehyde, 277, 293, 297, 312, 328, 335
— , enol-acetate of, 295, 368
*iso*Camphenilanaldehyde, 294, 309
Camphenilanaldoxime, 312
Camphenilane, **278**
— , nitro-derivatives of, 279
Camphenilanic acid, 277, 294
*iso*Camphenilanic acid, 277, 294
Camphenilanol, 295
Camphenilene, 245
Camphenilic nitrite, *see* ω-Nitrocamphene
Camphenilol, 248, 294
— , dehydration of, 246, 370
— , derivatives of, 369
— , stereoisomers of, 369
*iso*Camphenilol, 245
Camphenilone, 279, 284, 293, 297, 300, 303, **367**
— , action of methyl magnesium iodide on, 289, 317, 318
— , action of phosphorus pentachloride on, 331
— , action of sodamide on, 566
— dichloride, 371
— hydrazone, 278, 332, 372
— , oxidation of, 371
— oxime, 371
— , physical properties of, 369
— , pinacone from, 370
— , reduction of, 369
— semicarbazone, 369
— , synthesis of, 367
*iso*Camphenilone, 245
Camphenilonecarboxylic acid, 344
Camphenilylamine, 370
Camphenilylcarbinol, 276
Camphenilyl chloride, 245, 370
Camphenone, *see* β-Peri*cyclo*camphanone
α-Camphenone, 315
Camphenonic acid, 300, 568
Camphenylic acid, 284, 288, 297, 298
Campherol, 429
Camphidine, 492
α-Camphidone, 492
β-Camphidone, 492
Camphinene, 314
Camphoceenic acid, 372
*iso*Camphodiene, 314
Camphogene, 280
Camphol, 350
Campholactone, *see* Laurolactone
α-Campholactone, 383
Campholaldehyde, 444
Campholanic acid, 439, 444
— acid, amide, 444
— acid, identity of, with dihydro-α-campholenic acid and *iso*campholic acid, 444
Campholcarbinol, 444
α-Campholenaldehyde, 142, 392
α-Campholenamide, 438
Campholene, 439, 440
α-Campholenic acid, 119, 120, 388, 408, 420, **438**
— acid, reduction of, 444
β-Campholenic acid, 437, 439
β-Campholenamide, 418, 437, 439
*cyclo*Campholenic acid, 417
α-Campholenonitrile, 438
β-Campholenonitrile, 439
Campholic acid, 364, 367, 443
— acid, amide, 443
*iso*Campholic acid, *see* Campholanic acid
α-Campholide, 378, 392, 444, 480, 492
β-Campholide, 471, 484
α-Campholonic acid, 120, 438
α-Campholytic acid, 486, 501, 502
— acid, dibromide, 505
— acid, hydrobromide, 504, 505, 507
— acid, isomerisation into *iso*lauronolic acid, 505
β-Campholytic acid, *see* *iso*Lauronolic acid
*iso*Campholytic acid, *see* *iso*Lauronolic acid
α-Campholytolactone, 494, 503, 504
Camphonanic acid, 484
β-*iso*Camphone, 278
Camphonenic acid, 496, 509
Camphonic acid, 406

Camphonic acid, semicarbazone, 406
Camphonolactone, 483, 509
Camphonolonic acid, 483
Camphononic acid, 381, 481, 486
— acid, synthesis of, 483
Camphor, **373**
— , action of bromine on, 400
— , action of dehydrating agents on, 394
— , action of Grignard reagent on, 446
— , action of phosphorus pentachloride on, 433
— , action of sodium acetylide on, 447
— , alkyl derivatives of, 456
— azine, 446
— , constitution of, 374
— "cyanohydrin", 441
— α-dichloride, *see* α-Dichlorocamphane
— β-dichloride, *see* β-Dichlorocamphane
— 2:4-dinitrophenylhydrazone, 384
— enol, ethyl ether, 447
— , formation by oxidation of camphene, 296
— , formation from hydroxycamphene, 313
— glycol (*see also* 2:3-Dihydroxycamphane), 467
— , halogen derivatives of, **395**
— hydrazone, 273, 334, 446
— , hydroxymethylene derivative, *see* Hydroxymethylenecamphor
— , interconversion into epicamphor, 521
— , interconversion of enantiomorphs, **522**
— , manufacture from pinene, 386
— menthydrazone, 385
— , nitro-derivatives of, **410**
— , nomenclature of substitution products of, 386
— , oxidation of, 391–4, 466
— phenylsemicarbazone, 384
— , physical constants of, 384, 385
— , pinacone from, 391
— , reactions involving the α-carbon atom in, **447**
— , reactions of carbonyl group in, **433**
— , reduction of, 350, 365, 391
— , resolution of, 385
— semicarbazone, 383
— , sodium derivative of, 448
Camphor, stereochemistry of, 384
— , structure of the 'β' substitution products, 387
— , sulphonation of, mechanism of, 425
— , synthesis of, 383
*iso*Camphor, 441, 576
π-Camphor, *see* Dihydroteresantalal
ω-Camphor, 432
α-Camphoramic acid, 489
β-Camphoramic acid, 490
Camphoranil, 446
Camphor-3-carboxylic acid, 324, 402, 405, 410, 449–454, 521
— acid, methyl ester, 452
— acid, nitrile, *see* α-Cyanocamphor
Camphor-4-carboxylic acid, 523, 524
— acid, amide, 432
Camphordiazoaminobenzene, 416
Camphor-3-dithiocarboxylic acid, 465
Camphorenic acid, 406
Camphoric acid, 286, 326, 341, **478**
— acid, action of fused alkali on, 493
— acid, action of sulphuric acid on, 499
— acid, α- and β-amides, 489, 490
— acid, constitution of, 377
— acid, degradation products of, **502**
— acid, diamide, 488
— acid, dinitrile, 489
— acid, isomeric esters of, 485
— acid, monoethyl ester, 448
— acid, monomethyl esters, 482, 484, 485
— acid, oxidation of, 380, 493
— acid, reduction of, 492
— acid, *sec.*-semialdehyde, 428
— acid, *tert.*-semialdehyde, 428, 471
— acid, stereoisomers of, 479
— acid, synthesis of, 382
*iso*Camphoric acid, 479
Camphoric acid-π-sulphonic acid, 425, 499
— acid-π-sulphonyl bromide, 499
— acid-π-sulphonyl chloride, 499
Camphoric anhydride, 480
— anhydride, action of aluminium chloride on, 494

Camphoric anhydride, action of hydroxylamine on, 412
— dialdehyde, 467
Camphorimide, 490, 492, 520
Camphorimine, 441
α-Camphornitrilic acid, 474, 488, 490
β-Camphornitrilic acid, 491
α-Camphornitrilic-β-amide, 489
Camphorone, 493
Camphoronic acid, 379, 393, 483
— acid, synthesis of, 393
*iso*Camphoronic acid, 119, 121, 122, 125, 277, 389, 393, 563
*cycloiso*Camphoronic acid, 417
Camphoroxime, 383, 402, 434
, action of hypobromite on, 313
— , action of nitrous acid on, 441
— , Beckmann transformation of, 437
— , oxidation of, 436
Camphorquinone, 391, 411, 414, **466**
— , action of ammonia and amines on, 470, 477
— , action of bromine on, 468
— , action of diazomethane on, 470
— , action of Grignard reagent on, 469
— , action of hydrogen cyanide on, 469
— , action of sulphuric acid on, 469
— dioximes, 402, 477
— hydrazone, 416
— monoxime, *see iso*Nitrosocamphor and *iso*Nitrosoepicamphor
oximes, *N*- and *O*-derivatives of, 474, 475
— oximes, stereochemistry of, 472-7
— , reduction of, 467
*iso*Camphorquinone, 469
Camphor-π-sulphonamide, 422
Camphor-ω-sulphonamides, 420
Camphor-ω-sulphonanilide, 422
Camphorsulphonic acids, **419**
— acids, mechanism of formation of, 425
Camphor-"β"-sulphonic acid, *see* Camphor-ω-sulphonic acid
Camphor-π-sulphonic acid, 422
Camphor-π-sulphonic acid, reduction of, 423
Camphor-ω-sulphonic acid, 419
— acid, amine salts of, 421
— acid, oxime, 419
acid, reduction of, 420
— acid, structure of, 389
Camphor-π-sulphonyl bromide, 405
— chloride, 400, 422
Camphor-ω-sulphonyl chloride, 420
Camphor-π-thiol, 423
Camphorylacetoacetic ester, 488
Camphorylazoimide, 415
Camphorylcarbamide, 414
Camphoryl-ψ-carbamide, 414
Camphorylcarbinol, 459
Camphorylidenepropionic acid, 461
Camphorylmalonic ester, 488
Camphoryloxime, 412
Camphoryl-ψ-semicarbazide, 415
Camphotricarboxylic acid, 498
Camphylamine, 436
α-Camphylic acid, 500
β-Camphylic acid, 500
Camphylisoxazole, *see* α-Cyanocamphor
Carane, **61**, 69, 83
— , action of bromine on, 63
— , action of halogen acids on, 63
— , physical constants of, 62
— , reduction of, 63
— , synthesis of, 62
Carbocamphenilone, 288
Carbofenchonone, 288, 578
— , oxime, 578
— , quinoxaline derivative, 578
Carboxyapocamphoric acid, 277, 301, 390
γ-Carboxylocamphenehydratolactone, 325
Carene glycols, 69
— oxides, 70
Δ^3-Carene, **64**
— , action of bromine on, 72
- , constitution of, 65
— , dehydrogenation of, 69
— nitrosate, 69, 72
— nitrosochloride, 72
— , oxidation of, 65, 68-71
— , physical constants of, 69
— , reduction of, 62, 69
Δ^4-Carene, **73**
— , action of hydrogen chloride on, 76
— , action of maleic anhydride on, 76

Δ^4-Carene, colour reaction of, 76
— , constitution of, 73
— from piperitenone hydrazone, 75
— , oxidation of, 73, 76
— , physical constants of, 75
— , synthesis of, 75
Δ^3-Carene-5:6-epoxide, **95**
— , constitution of, 95
— , conversion into dichloro- and dibromo-menthones, 98
— , formation of geranic acid from, 96
— , isomerisation of, 98
— , oxidation of, 95
— , physical constants of, 97
— , reduction of, 95
Carol, 81
— , methyl xanthate of, 75
Carone, **77**
— , action of ammonium hydrogen sulphide on, 84
— , action of hydrogen bromide on, 81
— , action of sulphuric acid on, 81
— , bisnitroso-derivative, 84
— , constitution of, 77
— cyanohydrin, 85
— hydrazone, 61, 83
— , isomerisation to carvenone, 79, 81
— , oxidation of, 78
— oxime, 81
— , physical constants of, 79
— , reduction of, 79
— semicarbazone, 79, 82
— thiosemicarbazone, 82
Caronic acids, 65, 70, 74, 78
Carvenone, 79, 81, 83
Carvomenthol, 35, 80
Carvone hydrobromide, action of alkali on, 86
'Carvopinone', 183, 185, 240
Carvotanacetone, 35
Carvoxime hydrochloride, 181
Carylamine, 81
Chamaecyparis formosensis Matsum, oil from, 210
3-Chloro-2-aminocamphane, 414
N-Chloroaminocamphor, 416
4-Chloro*iso*borneol, 522
?-Chloro*iso*borneol, 309
4-Chloro*iso*bornyl bromide, 304, 523
— chloride, *see* β-Dichlorocamphane
Chlorobromocamphane, 303
α-Chloro-α′-bromocamphor, 397
α′-Chloro-α-bromocamphor, 397
α-Chloro-π-bromocamphor, 424
π-Chloro-α-bromocamphor, 425
2-Chlorocamphane, *see* Bornyl and *iso*bornyl chlorides
3-Chlorocamphane, 329
?-Chlorocamphane, 330
2-Chlorocamphane-4-carboxylamide, 442
2-Chlorocamphane-2-carboxylic acid, 344
2-Chlorocamphane-4-carboxylic acid, 346
2-Chlorocamphan-8-ol, 270
α-Chlorocamphene, 303, 522
β-Chlorocamphene, 304, 339
ω-Chlorocamphene, 303
1-Chlorocamphene, *see* α-Chlorocamphene
4-Chlorocamphene, *see* β-Chlorocamphene
α-Chlorocamphenilone, 303
β-Chlorocamphenilone, 304
α-Chlorocamphor, 396
— , mutarotation of, 397
α′-Chlorocamphor, 397
π-Chlorocamphor, 400, 423
ω-Chlorocamphor, 399
4-Chlorocamphor, 523, 524
α-Chlorocamphor-α′-carboxylic acid, 396, 449
α-Chlorocamphoric acid, methyl ester, 496
— acid, phenyl ester, 496
α-Chlorocamphoric anhydride, 495
π-Chlorocamphoric anhydride, 499
α-Chlorocamphor-π-sulphonic acid, 424
α-Chlorocamphor-ω-sulphonic acid, 422
π-Chlorocamphor-π-sulphonic acid, 423
α-Chlorocamphor-π-sulphonyl bromide, 424
α-Chlorocamphor-π-sulphonyl chloride, 400, 424
π-Chlorocamphor-π-sulphoxide, 423
ω-Chlorocamphor-ω-sulphoxide, 389
α-Chloro-α-cyanocamphor, 455
α-Chloro-α′ω-dibromocamphor, 399
Chlorodihydrodimethylpinylamine, 190
6-Chloroepicamphor, 518
?-Chloroepicamphor, 328
Chlorofenchene, 573, 585
Chloromethylenecamphor, 460

2-Chloro-2-nitrocamphane, 436
α-Chloro-α′-nitrocamphor, 399, 410
α′-Chloro-α-nitrocamphor, 399
2-Chloropinane, 104
7-Chloropinane, 104, 198, 212
ω-Chlorotricyclene, 336
4-Chlorotricyclene, 304, 338
Chrysanthemum sinense, oil from, 373
Cinnamomum camphora Nees, oil from, 373
Cumic acid, 193, 204
3-Cyanocamphonanic acid, *see* α-Camphornitrilic acid
α-Cyanocamphor, 377, 454, 465
Cyanocarone, 85
Cyanodihydro-α-campholytic acid, *see* β-Camphornitrilic acid
Cyclene, *see* Tricyclene
*iso*Cyclenone, *see* β-Peri*cyclo*camphanone
Cyanomarathrum nuttalii, oil from, 192

D

Dacrydium Franklini Hook, oil from, 73
Darwinia grandiflora, oil from, 210
Dehydrocamphenic acid, 125, 299
N-Dehydrocamphidines, 322
Dehydrocamphoric acid, 496
— acid, methyl ester, 496
*iso*Dehydrocamphoric acid, 496
Dehydro*iso*fenchocamphoric acid, 582, 584
— acid, oxidation of, 584
— acid, synthesis of, 584
Dehydrohomocamphoric acid, 378, 482
Dehydrosantenic acid, 255
2-Deuterocamphane, 274
1:3-Diacetyl*cyclo*pentane, 243, 250
— , properties of, 244
2:3-Diaminocamphane, 477
Diazocamphor, 416
Dibornyl, 343
Dibornylamine, 436
Dibornyl ether, 363
2:6-Dibromocamphane, *see* Bornyl dibromide
2:10-Dibromocamphane(?), 306
Dibromocampholide, 405
αα′-Dibromocamphor, 381, 401, 405, 448
απ-Dibromocamphor, 405, 408, 425
α′π-Dibromocamphor, 409
αω-Dibromocamphor, 401, 404, 407, 439
α′ω-Dibromocamphor, 404, 407
αα′-Dibromocamphor-π-sulpholactone, 425
α′ω-Dibromocamphor-α-sulphonamide, 404
αα′-Dibromocamphor-π-sulphonic acid, 425
1:8-Dibromocarvomenthone, 82
*iso*Dibromodihydro-β-camphylic acid, 501
Dibromodihydroumbellulone, 59
1:8-Dibromomenthone, 95
— , conversion into piperitone, 95
απ-Dibromo-α′-nitrocamphor, 409, 413
αω-Dibromo-α′-nitrocamphor, 404, 407, 412, 414
Dicamphoryl peroxide, 493
α-Dichlorocamphane, 303, 322, 433, 522
β-Dichlorocamphane, 304, 338, 433
2:2-Dichlorocamphane, *see* α-Dichlorocamphane
2:3-Dichlorocamphane, 274, 326, 328
2:4-Dichlorocamphane, *see* β-Dichlorocamphane
2:6-Dichlorocamphane, *see* Bornyl dichloride
2:10-Dichlorocamphane, 336
αα′-Dichlorocamphor, 399
απ-Dichlorocamphor, 400, 424
1:8-Dichlorocarvomenthone, 84
Dichloro-*p*-menthanediols, 202
1:2-Dichloro-*p*-menthane-6:8-diol, 173
2:8-Dichloro-*p*-menthane-1:6-diol, 176
2:3-Dideuterocamphane, 274
β-Difenchene, 551
Difencholylurea, 565, 566
Dihydrocamphene, *see* *iso*Camphane
β-Dihydrocamphoceenic acid, 371
Dihydro-α-campholenic acid, *see* Campholanic acid
Dihydro-β-campholenoiminolactone, 418, 437
Dihydro-β-campholenolactone, 437, 439, 440
Dihydro-α-campholenonitrile, 443
Dihydro-α-campholytic acid, 501
Dihydrocarvone hydrobromide, conversion into carone, 77
— hydrobromide, formation from carone, 81
Dihydrocumic acids, 193
α-Dihydroeucarveol, 87, 91
— , action of phosphorus pentachloride on, 93
α-Dihydroeucarvone, 87, 91
β-Dihydroeucarvone, 91
β-Dihydroeucarvoxime, 91

α-Dihydroeucarvylamine, 94
Dihydro-α-fencholenic acid, 574, 577
— acid, nitrile, 577
Dihydro-β-fencholenic acid (*see also* Fencholic acid), 574
Dihydrolaurolenic acid, *see* Laurolanic acid
Dihydro*iso*lauronolic acid, 501, 507, 508
Dihydromyrtenal, 200, 212, 224, 231
Dihydromyrtenic acid, 226
Dihydromyrtenol, 210, 212
— , *cis*- and *trans*- forms of, 212
Dihydromyrtenylmethylcarbinol, 201
Dihydrosabinol, 31
Dihydroteresantalal, 271, 432
Dihydroteresantalic acid, 267
Dihydro*iso*teresantalic acid, 270
Dihydroteresantalol, 271, 431
β-Dihydroumbellulol, 54, 57
α-Dihydroumbellulone, 59
β-Dihydroumbellulone, 55, 57
Dihydroverbenene, 219
Dihydroverbenol, 235
2:3-Dihydroxycamphane (*see also* Camphor glycol), 330
2:5-Dihydroxycamphane, 361, 430
2:6-Dihydroxycamphane, 337
Dihydroxy-β-campholenic acid, 440
Dihydroxydihydro-α-campholenic acid, 438
Dihydroxydihydro-α-campholytic acid, 504
Dihydroxydihydrolaurolenic acid, 510
αδ-Dihydroxy-α-methyl-δ-*iso*propyladipic acid, 21
αα′-Di-iodocamphor, 409
5:6-Diketoborneol, *see* 6-Hydroxycamphorquinone
p-Diketocamphane, 273, 361, 394, 429, 516, 524
2:3-Diketocamphane, *see* Camphorquinone
2:5-Diketocamphane, *see* *p*-Diketocamphane
2:6-Diketocamphane, 337, 362, 394, 438
αδ-Diketo-ββ-dimethylhexoic acid, 584
Dimercuricamphor di-iodide, 409
ββ-Dimethyladipic acid, 92
1:1-Dimethyl*cyclo*butane-2:4-dicarboxylic acid, *see* Norpinic acid
Dimethylcampholamide, 457
Dimethylcampholide, 502
αα′-Dimethylcamphor, 457
αα-Dimethylglutaconic acid, 499
αα-Dimethylglutaric acid, 440
αε-Dimethyl-Δ^{δ}-heptenoic acid, 490
1:3-Dimethyl*cyclo*hexane, 492
1:1-Dimethyl-Δ^{3}-*cyclo*hexen-2-one-4-carboxylic acid, *see* *iso*Lauronic acid
1:3-Dimethyl-1-hydroxy*cyclo*hexane-4-carboxylic acid, 494
Dimethylnorcampholide, 286
ββ-Dimethylpimelic acid, 88
1:1-Dimethyl*cyclo*propane-2:3-dicarboxylic acid, *see* Caronic acid
αα-Dimethylpropane-αβδ-tricarboxylic acid, 468
1:2-Dimethyl-3-*iso*propyl*cyclo*pentane, 6, 8, 10, 13, 20, 46, 50
2:3-Dimethyl-4-*iso*propyl*cyclo*pentanol, 42
2:3-Dimethyl-4-*iso*propyl*cyclo*pentanone, 42
2:3-Dimethyl-4-*iso*propyl-Δ^{2}-*cyclo*pentenol, 31
2:3-Dimethyl-4-*iso*propyl-Δ^{2}-*cyclo*pentenone (*see also* "Isothujon"), 31
Dimethyltricarballylic acid, 119, 122, 563
Dimyrtenyl, 213
2:3-Dinitrocamphane, 328
ωω-Dinitro-ω-chlorocamphor, 389
ωω-Dinitro-2-hydroxycamphane, 312
Dipentene dihydrochloride, 65
Dipentene, formation from α-pinene, 112, 133, 134, 136
Dipentene hydrochloride, 196
α-Dipinene, 166
Dryobalanops aromatica Gaertn., oil from, 349

Endoborneol, 329, 358
Endocamphene, 287
Epiborneol, 328, 430, 517
— , 3:5-dinitrobenzoate, 358, 518
— , phenylurethane, 517
— , synthesis of, 358
*iso*Epiborneol, 518
— , 3:5-dinitrobenzoate, 518
— , phenylurethane, 518
Epiborneol-2-carboxylic acid, 520
Epiborneol-3-carboxylic acid, *see* 3-Hydroxycamphane-3-carboxylic acid
Epibornyl chloride, *see* 3-Chlorocamphane
Epicamphor, 512, 524
— , action of Grignard reagent on, 521
— , interconversion into camphor, 521
— , oxidation of, 466, 518
— oxime, 517
— , physical constants of, 517
— , reduction of, 517

Epicamphor, semicarbazone, 517
Epicamphor-2-carboxylic acid, 520
Epicamphor-6-carboxylic acid, 520
Epi*iso*fenchone, 585, 586
— , oxime, 586
— , semicarbazone, 585
2-Ethoxybornylene, 447
Ethynylbornyl alcohol, 447
Eucalyptus globulus, oil from, 210, 221, 223, 240, 531
Eucarvone, **85**
— , action of methyl magnesium iodide on, 94
— , action of phosphorus pentachloride on, 93
— , benzylidene derivative, 88, 94
— , colour reaction of, 91
— , constitution of, 86
— 2:4-dinitrophenylhydrazone, 91
— hydroxylamino-oxime, 94
— , maleic anhydride adduct, 91
— , oxidation of, 86
— , physical constants of, 91
— , pinacones from, 93
— , reduction of, 87, 88, 91, 93
— semicarbazone, 91
Eucarvoxime, 94
Euterpene, 93

False camphor wood oil, 223
Fenchane, **526**, 528
— , action of nitric acid on, 526
α-Fenchane, *see iso*Bornylane
β-Fenchane, 530
Fenchane-3-carboxylic acid, 586
Fenchenes, **531**
— , formation from fenchyl and *iso*fenchyl alcohols, 536
— , general preparation of, 536
— , nomenclature of, 534
α-Fenchene, 530, 535, **538**
— , constitution of, 539
— , conversion into β- and γ-fenchenes, 541
— dibromide, 527, 539, 542, 551
— hydrate, *see* Methyl-α-fenchocamphorol
— , hydration of, 543, 557, 580
— hydrochloride, 541
— , oxidation of, 539, 542
— , physical constants of, 539
— , reduction of, 528, 541
— , synthesis of, 540
β-Fenchene, 535, **543**
— dibromide, 544
— hydrate (*see also* Methyl-β-fenchocamphorol), 545, 551, 559
— hydrate, phenylurethane, 559, 560
— , hydration of, 546, 558
— hydrochloride, 546
— nitrosochloride, 544
— , oxidation of, 544, 545
— , physical constants of, 544
γ-Fenchene, 535, 545, **547**
— , adduct with phenylazide, 548
, hydration of, 548
— nitrosate, 548
— nitrosochloride, 548
δ-Fenchene, 535, 547, **548**
— , adducts with phenylazide, 549
— nitrosate, 548
— nitrosochloride, 548
— , oxidation of, 548
ε-Fenchene, *see* 1-Methylsantene
ζ-Fenchene, 538, **549**
— hydrochloride, 550
*cyclo*Fenchene, 276, 536, **550**, 573
— as intermediate in fenchyl—*iso*fenchyl isomerisation, 165, 538, 558
— , hydration of, 551, 558
— hydrochloride, 541, 551
— , isomerisation of, 551
— , reduction of, 551
δ-Fenchene-3-carboxylic acid, 586
Fenchenylanaldehyde, 542
α-Fenchenylanic acid, 541
— acid, synthesis of, 542
*iso*Fenchocamphononic acid, 583
— acid, semicarbazone, 583
— acid, synthesis of, 583
*iso*Fenchocamphoric acid, 527, 547, 548, 581, 585
— acid, stereoisomers of, 582
— acid, synthesis of, 583
*iso*Fenchocamphoric anhydride, 582
α-Fenchocamphorol, 246, 370, 542
β-Fenchocamphorol, 246, 332, 370, 545
— , hydrogen phthalate, 545
— , phenylurethane, 545
β-*iso*Fenchocamphorol, 545

β-*iso*Fenchocamphorol, hydrogen phthalate, 545
α-Fenchocamphorone, 246, 535, 539, 562
— semicarbazone, 539
— , synthesis of, 540
β-Fenchocamphorone, 246, 279, 332, 535, 544
— hydrazone, 278
— , synthesis of, 545
α-Fenchocarboxylic acid, 578
β-Fenchocarboxylic acid, 579
Fencholamide, 564
— , partial synthesis of, 565, 566
*iso*Fenchol-3-carboxylic acid, 586
α-Fencholenic acid, 572, 574
— acid, amide, 574
β-Fencholenic acid, 574
— acid, amide, 575
γ-Fencholenic acid, 572
α-Fencholenonitrile, 574
β-Fencholenonitrile, 574
Fencholic acid, 564, 576
*iso*Fencholic acid, 581
Fenchone, 527, 553, **560**
— , action of Grignard reagent on, 579
— , action of halogens on, 572
— , action of nitric acid on, 570
— , action of phosphorus pentachloride on, 572
— , action of sodamide on, 564
— , action of sodium and carbon dioxide on, 578
— , constitution of, 561
— , dehydration of, 561
— dichloride, 573
— hydrazone, 527, 550, 573
— , oxidation of, 561, 570
— oxime, 561, 569, 574
— oxime, action of nitrous acid on, 576
— oxime, action of sulphuric acid on, 574
— oxime, reduction of, 577
— . physical constants of, 569
— , reduction of, 528, 552, 569
— semicarbazone, 569
— , stereochemistry of, 385
— , synthesis of, 566
*iso*Fenchone, 527, 559, **580**
— , action of bromine on, 585
— , action of Grignard reagent on, 587
— , action of phosphorus pentachloride on, 585
*iso*Fenchone, action of sodium and carbon dioxide on, 586
— , constitution of, 581
— hydrazone, 527, 585
— , oxidation of, 581, 585
— oxime, 585
— , physical constants of, 585
— , reduction of, 585
— semicarbazone, 584
— , synthesis of, 584
iso-Fenchone-3-carboxylic acid, 586
Fenchoneimine, 576
— , ring fission of, 576
*iso*Fenchonequinone, 585
Fenchopinacone, 570
Fenchosantenone, 567
— oxime, 568
— semicarbazone, 568
Fenchyl alcohol, 156, 199, 203, **552**
— alcohol, conversion into fenchyl chloride, 555
— alcohol, dehydration of, 164, 246, 263, 536, 539, 547, 548, 556
— alcohol, formation of *iso*fenchyl alcohol from, 164
— alcohol, hydrogen phthalates, 553
— alcohol, *p*-nitrobenzoates, 553
— alcohol, oxidation of, 553, 554
— alcohol, phenylurethanes, 553
— alcohol, physical constants of, 553
— alcohol, picrate, 190, 203
— alcohol, reduction of, 529, 554
— alcohol, stereoisomers of, 553
— alcohol, *p*-toluenesulphonate, 549, 556
α- and β-Fenchyl alcohols, *see* Fenchyl alcohol, stereoisomers of
*iso*Fenchyl alcohol, 543, 546, 548, 551, **557**
alcohol, benzoate, 559
alcohol, dehydration of, 536, 543, 559
alcohol, hydrogen phthalate, 559
alcohol, α-naphthylurethane, 558, 559
— alcohol, oxidation of, 559, 580
— alcohol, phenylurethane, 558, 559
— alcohol, physical constants of, 558
— alcohol, stereoisomers of, 559
α- and β-*iso*Fenchyl alcohols, *see* *iso*Fenchyl alcohol, stereoisomers of

Fenchylamine, 577
— , action of nitrous acid on, 539, 578
— , *N*-acyl derivatives of stereoisomers, 577
Fenchyl chloride, 533, 555
— chloride, action of bases on, 539, 543, 555
*iso*Fenchyl chloride, 559
— chloride, action of bases on, 544, 559
Fenchylene, *see* δ-Fenchene
*iso*Fenchylone, *see* δ-Fenchene
*iso*Fenchyl ethyl ether, 558
Fennel, oil of, 560
Ferula galbaniflua, oil from, 191
Foeniculus vulgare, oil from, 560
π-Formyl-π-apocamphor (*see also* π-Ketocamphor), 431

Geranic acid, formation from Δ^{3}-carene-5:6-epoxide, 96

Hernandia peltata Meissn., oil from, 223
Hexamercuripentacamphor di-iodide, 410
R-Homoamino*iso*camphanes, 296
Homoapofenchocamphoric acid, synthesis of, 545, 546
R-Homocamphenilols, 287, 296
R-Homocamphenilones, 287, 295
Homocamphor, 470
— oxime, 470
β-Homocamphor, *see* Homoepicamphor
Homocamphoric acid, 377, 449, 455, 461, 481
β-Homocamphoric acid, 514
Homocamphoronic acid, 381, 406
— acid, methyl ester, 483
Homocamphorquinone, 470, 472
Homocaronic acid, 68, 95
Homoepicamphor, 516
Homo*iso*fenchocamphoric acid, 584
Homopinene, 214
Homopinocamphoric acid, 128
*iso*Homopinocamphoric acid, 236
Homosantenic acid, 258, 263
Homoterpenylformic acid, 117, 155
Homoterpenylic acid, 74, 117, 155, 192
Homoterpenyl methyl ketone, 37, 70, 115, 149
Homothujadicarboxylic acid, 15, 51, 55
Hydrochloroteresantalic acid, 267
5-Hydroxyborneol, *see* 2:5-Dihydroxycamphane
6-Hydroxyborneol, *see* 2:6-Dihydroxycamphane
1-Hydroxy-8-bromocarvomenthone, 82
2-Hydroxycamphane, *see* Borneol and *iso*Borneol
3-Hydroxycamphane, *see* Epiborneol
1-Hydroxy*iso*camphane, 359
2-Hydroxycamphane-4-carboxylic acid (*see also* Borneol-4-carboxylic acid), 344
3-Hydroxycamphane-3-carboxylic acid, 517
2-Hydroxycamphane-π-sulphonic acid, 423
2-Hydroxycamphane-ω-sulphonic acid, 420
Hydroxy-π-camphanic acid, 498
1-Hydroxycamphene, 313, 388, 399, 425
6-Hydroxycamphene, 337
4-Hydroxycamphene-1-carboxylic acid, 524
Hydroxycamphenic acid, 299
Hydroxycampholic acid, 481
Hydroxy-β-campholide, acetate, 484
Hydroxycamphors, 427
α-Hydroxycamphor, 428, 429, 524
— semicarbazone, 428
"β-Hydroxycamphor", *see* 2-Hydroxyepicamphor
π-Hydroxycamphor, 430
— hydrazone, 270
— semicarbazone, 271, 430, 431
ω-Hydroxycamphor, 432
— semicarbazone, 432
3-Hydroxycamphor, *see* α-Hydroxycamphor
4-Hydroxycamphor, 432, 524
5-Hydroxycamphor, 417, 429
— semicarbazone, 429
6-Hydroxycamphor, acetate of, 363
3-Hydroxycamphor-3-carboxylic acid, 427
5-Hydroxycamphor-5-carboxylic acid, 516
π-Hydroxycamphoric acid, 498
ω-Hydroxycamphoric acid, 498
4-Hydroxycamphoric acid, 496
5-Hydroxycamphoric acid, 362, 363
4-Hydroxycamphorolactone, 496
Hydroxy*iso*camphoronic acid, lactone, 119
6-Hydroxycamphorquinone, acetate, 362, 363
8-Hydroxycarvomenthone, 80, 81
Hydroxycarvomenthone nitrosylic acid, 84
8-Hydroxycarvotanacetone, 138, 143

4-Hydroxy-3:4-dehydrohomocamphor, *see* Homocamphorquinone
Hydroxydihydro-α-campholytic acid, 503, 504
Hydroxydihydrocarvoxime, 186, 188
Hydroxydihydro-α-fencholenic acid, 577
Hydroxydimethylsuccinic acid, 119, 123
6-Hydroxyepiborneol, *see* 2:5-Dihydroxycamphane
2-Hydroxyepicamphor, 428, 470, 524
6-Hydroxyepicamphor, 361
Hydroxy-α-fenchenic acid, 535, 539, 555, 562
Hydroxy-β-fenchenic acid, 535, 544
α-Hydroxy*iso*fenchocamphoric acid, 582
Hydroxyfenchones, 570
Hydroxy*iso*fenchone, 585
Hydroxymethylenecamphor, 458–62
— , action of bromine on, 401, 460
— , action of hydroxylamine on, 454, 461
— , oxidation of, 460
— , reduction of, 459
— , structure of, 459
3-Hydroxymethylene*iso*fenchone, 585
Hydroxymethylenesantenone, 262
Hydroxymethylenethujone, 35, 51
Hydroxypinic acid, 115, 151
Hydroxypinocamphone, 147, 206
— oxime, 189
2-Hydroxyverbenone, 237
Hyssop, oil of, 205, 226
Hyssopus officinalis, oil of, 206, 226

Iminobenzoylcamphor, 465
α-Iminocamphor, 415, 470
Iminohomocamphor, 472
Infracampholenic acid, 437
α-Iodocamphor, 409
α-Iodo-α-formylcamphor, 409
"Isothujon", 31, 39–43, 46, 47
— oxime, 49
"Isothujylamin", 48

Juniperis Sabina L., oil from, 16, 28

Kaempferia galanga, oil from, 65
3-Ketoborneol, *see* 2-Hydroxyepicamphor
5-Ketoborneol, *see* 6-Hydroxyepicamphor
6-Ketoborneol, *see* 6-Hydroxycamphor
α-Keto-α-campholenic acid, 439
π-Ketocamphor (*see also* π-Formyl-π-apocamphor), 258, 431, 432
ω-Ketocamphor, 432
3-Ketocamphor, *see* Camphorquinone
5-Ketocamphor, *see* *p*-Diketocamphane
6-Ketocamphor, *see* 2:6-Diketocamphane
*iso*Ketocamphoric acid, 119, 121, 127, 438
α-Keto*iso*camphoronic acid, 123, 124, 127
δ-Keto-β-carboxy-γγ-dimethylhexoic acid, 504
2-Ketoepiborneol, *see* α-Hydroxycamphor
6-Ketoepiborneol, *see* 5-Hydroxycamphor
2-Ketoepicamphor, *see* Camphorquinone
6-Ketoepicamphor, *see* *p*-Diketocamphane
Ketofenchone, 570
Keto*iso*lauronolic acid, 508
Ketonopinone, 150
Ketopinic acid, 300, 301, 312, 341, 389, 432
*iso*Ketopinic acid, 267, 269, 357, 423, 430
— acid, hydrazone, 270
— acid, semicarbazone, 268
Ketothujane, 7
γ-Keto-αββ-trimethylvaleric acid, 393

Laurenone, 510
Laurolactone, 511
Laurolanic acid, 511
Laurolene, 492, 512
*iso*Laurolene, 494, 504, 508
Laurolenic acid, 486, 509
*iso*Lauronic acid, 506
Lauronolic acid, *see* Laurolenic acid
*iso*Lauronolic acid, 437, 486, 494, 499, 505–8
— acid, action of hydrogen bromide on, 505
— acid, synthesis of, 508
γ-Lauronolic acid, *see* Camphonenic acid
*iso*Lauronolonitrile, 495
Lavandula dictata, oil from, 561
Lavandula pedunculatum, oil from, 373

m-Menthadiene, 64
p-Menthane-1:2:6:8-tetrol, 138, 175
p-Menthane-1:2-8-triol, 82

$\Delta^{3(8)}$-*m*-Menthene, 63
Δ^{1}-*p*-Menthene-4:6-diol, 32
Δ^{1}-*p*-Menthene-4:6:7-triol, 28
Δ^{1}-*o*-Menthen-3-one, 237
4-Methoxy-3:4-dehydrohomocamphor, 470
2-*N*-Methylaminocamphane-ω-sulphonic acid, 421
3-Methylaminocamphor, 470, 474
2-Methylaminoepicamphor, 470
Methylanilomethylenecamphor, 459
tert.-Methylborneol, 446, 580
Methyl bornylxanthate, 324, 364
tert.-Methylepiborneol, 580
3-Methylepiborneol, 560
Methyl epibornylxanthate, 326, 518
α-Methylcamphene, 290, 580
Methylcamphenilol, 289, 317
— , dehydration of, 318
Methyl camphenilylxanthate, 331
Methylcampholenol, 141
α-Methylcamphor, 453, 456
3-Methylcamphor-3-carboxylic acid, 453
— acid, methyl ester, 453
α-Methyl-α-cyanocamphor, 455
α-Methylenecamphor, 456
1-Methyl-α-fenchene, 290, 580
4-Methyl-α-fenchene, 521, 560
1-Methyl-β-fenchene, 587
1-Methyl-γ-fenchene, 587
— nitrosochloride, 587
4-Methyl-γ-fenchene, 521
2-Methyl-δ-fenchene, *see* 1-Methyl-γ-fenchene
Methyl-α-fenchocamphorol, 530, 539, 540
— , dehydration of, 541
— , phenylurethane, 540
Methyl-β-fenchocamphorol (*see also* β-Fenchene hydrate), 545
— , dehydration of, 545
3-Methyl*iso*fenchone, 586
— oxime, 586
— semicarbazone, 586
tert.-Methylfenchyl alcohol, 290, 580
2-Methyl*iso*fenchyl alcohol, 587
4-Methyl*iso*fenchyl alcohol, 560
Methyl fenchylxanthate, 539, 556
— fenchylxanthate, amide, 556
Methyl *iso*fenchylxanthate, 548, 560
— *iso*fenchylxanthate, amide, 560
1-Methyl-Δ^{2}-*cyclo*hexen-3-one, 233
α-Methylhomocamphoric acid, 454
Methylmyrtenyl, 214
Methylnopinol, 103, 196
1-Methylnorcamphor, 567
3-Methylnorcamphor, 249, 256
β-Methylpentane-βγε-tricarboxylic acid, 97, 468
1-Methyl*cyclo*pentan-3-one-1-carboxylic acid, 566, 575
Methylpinocamphoneoxime, 190
Methyl pinocamphylxanthate, 209
Methyl*cyclo*propane-1:2:3 tricarboxylic acid, 191
α-Methyl-α′*iso*propyladipic acid, 8
α-Methyl-β-*iso*propylglutaric acid, 41
1-Methyl-3-*iso*propyl-Δ^{1}-*cyclo*hexen-6-one, *see* *iso*Camphor
1-Methyl-3-*iso*propylidene*cyclo*pentan-2-one, *see* Camphorone
1-Methylsantene, 263
sec.-4-Methylsantenol, 264
tert.-1-Methylsantenyl alcohol, 263
Methyl thujylxanthates, 11, 15, 27
Methyl verbanylxanthate, 217
Murraya Koenigii Spreng, oil from, 16
Myrtanal, *see* Dihydromyrtenal
Myrtanol, *see* Dihydromyrtenol
Myrtenal, 140, 185, 199, **223**
— 2:4-dinitrophenylhydrazone, 226
— , oxidation of, 226
— oxime, 224, 226
— phenylsemicarbazone, 226
— , physical constants of, 224
— , reduction of, 224
— semicarbazone, 226
Myrtenic acid, 224, 226
Myrtenol, 140, 185, 199, **210**
— , constitution of, 211
— , esters of, 214
— , halides derived from, 213
— , hydrogen phthalate, 210, 212
— , oxidation of, 211, 212
— , physical constants of, 212
— , reduction of, 212
— , urethanes, 212
Myrtenyl bromide, 213
— chloride, 210
— ethyl ether, 210
Myrtle oil, 210
Myrtus communis L., oil from, 210

Nametkin isomerisation, 162, 290, 304, 425, 522
"Ngai-camphor", 349

sec.-Nitro*iso*bornylane, 531
tert.-Nitro*iso*bornylane, 529
2-Nitrocamphane, 274, 436
Nitro*iso*camphane, 278
Nitro*iso*camphanyl cyanide, 312
α-Nitrocamphene, 314, 339
ω-Nitrocamphene, 311, 334
1-Nitrocamphene, 313
4-Nitrocamphenehydrato-π-sulpho-lactone, 314
Nitrocamphenilanes, 279
α′-Nitrocamphor, 402, 410
*pseudo*Nitrocamphor, 411
2-Nitrofenchane, 526
6-Nitrofenchane, 526
tert.-Nitro-β-fenchane, 530
sec.-Nitrofenchone, 571
tert.-Nitrofenchone, 571
Nitrolaurolactone, 511
Nitropinene, 204
α-*iso*Nitrosocamphene, 315
*iso*Nitrosocamphor, 377, 402, 410, 450, 466, 471, 490
— , configuration of stereoisomers, 472
— , *N*- and *O*- derivatives of, 474
*so*Nitrosoepicamphor, 475, 519
— , configuration of stereoisomers, 475
— , *N*- and *O*- derivatives of, 475
Nitrosopinene, 181–5, 227
— , phenylurethane, 181
*iso*Nitrososantenone, 261
Nitroterebenthine, 204
Nopinic acid, 117, 192, 201
α- and β-Nopinols, 196
Nopinolacetic acid, 196, 558
Nopinone, 117, 192
— , action of hydrogen chloride on, 194
— , action of sulphuric acid on, 195
— , benzylidene derivative, 194
— , chlorodibenzylidene derivative, 194
— , reduction of, 195
— semicarbazone, 194
Nopol, 205
Norborneol, 251, 356
π-Norborneol, 251, 257
Nor*iso*borneol, 251
π-Nor*iso*borneol, 251
π-Norbornylamine, 260
Norbornylene, 356
Norcamphane-2-carboxylic acid, 356
π-Norcampholenic acid, 260
Nor*iso*campholic acid, 445
Norcamphor, methylation of, 368
π-Norcamphor, 257
Norpinic acid, 115, 151, 153, 219
— acid, synthesis of, 154
Norpinic anhydride, 153

*allo*Ocimene, formation from α-pinene, 134
Olibanol, 214
Olibanum oil, 214
Origanene, 10

*cyclo*Pentane-1:3-dicarboxylic acid, 243
Percamphoric acid, 493
Peri*cyclo*camphane, 417
β-Peri*cyclo*camphanol, 417
β-Peri*cyclo*camphanone, 416, 430
Pernitrosocamphor, 440
Pernitrosofenchone, 576
*iso*Pernitrosofenchone, 576
Pernitrososantenone, 261
Phenylcamphenilol, 372
β-Phenylenebisiminocamphor, 477
3-Phenylhydroxycamphor, 469
2-Phenylhydroxyepicamphor, 469
Phenylhydroxyhomocampholic acid, 458
Phenyliminocamphor, 475
— oxime, 475
Pinacon-pinacolin transformations, 158
Pinane, **100**, 199, 236
— , *cis*- and *trans*- forms, 102
— , action of halogens on, 104
— , oxidation of, 103, 104
— , reduction of, 103
α-Pinene, **105**, 209, 210
— , action of aluminium chloride on, 178
— , action of bromine on, 168
— , action of *N*-bromosuccinimide on, 169
— , action of chlorine on, 167
— , action of ethyl diazoacetate on, 190
— , action of hydrogen chloride on, 170
— , action of hypochlorous acid on, 172
— , action of iodine on, 170
— , action of phenylazide on, 190
— , action of phosphorus halides on, 176
— , action of picric acid on, 190

α-Pinene, action of sulphur on, 178
— , action of thionyl chloride on, 176
— , constitution of, 106–27
— , conversion into bornyl chloride, 155
— , conversion into camphene, 135
— , conversion into myrtenal and myrtenol, 140
— , conversion into sobrerol, 137, 143
— , conversion into verbenol and verbenone, 139
— dibromide (*see also* Bornyl dibromide), 169
— dichloride (*see also* Bornyl dichloride), 167
— , formation from 2-chloropinane, 104
— , formation from β-pinene, 198
— , general reactions of, 165
— glycol, 147
— , hydration of, 155, 165, 554
— hydrochloride (*see also* Bornyl chloride), 171, 202
— hydroxylamino-oxime, 188
— , maleic anhydride adduct, 190
— , molecular rearrangements of, **156**
— nitrolamine, 180, 231
— nitrolanilide, 180
— nitrolbenzylamine, 132, 180
— nitrolpiperidide, 132, 180
— nitrosoazide, 186
— nitrosochloride, 132, 178
— nitrosochloride, conversion into nitrosopinene, 181
— nitrosochloride, reactions of, 179, 180, 185–90
— nitrosochloride, regeneration of α-pinene from, 180
— nitrosocyanide, 186
— , oxidation of, 112, **136**
— oxide, 141
— , purification *via* nitrosochloride, 180
— phosphorate, 139
— , physical constants of, 132
— , pyrolysis of, 133
— , reduction of, 100, 135
— , stereochemistry of, 385
— , synthesis of, 128
β-Pinene, **191**
— , action of formaldehyde on, 205
— , action of halogens on, 202
— , action of hydrogen chloride on, 202
β-Pinene, action of hypochlorous acid on, 202
— , constitution of, 192–7
— glycol, 201
— , hydration of, 202, 554
— , hydroferrocyanic acid compound, 205
— , isomerisation into α-pinene, 198
— nitrosite, 203
— , oxidation of, 199–202
— oxide, 200
— , physical constants of, 198
— , reduction of, 103, 199
— , synthesis of, 197
δ-Pinene, 104, 130, 209, 217, 219
*iso*Pinene, 549
— , identity with α-fenchene, 541
δ-Pinene-2-carboxylic acid, 228
Pinic acid, 115, 151, 211
— acid, stereochemistry of, 153
Pinocampheol, 104, **205**, 222
— , derivatives of, 209
— , oxidation of, 207, 230
— , stereoisomeric forms of, 207, 231
*iso*Pinocampheol, 207
*neo*Pinocampheol, 207
*neoiso*Pinocampheol, 207
Pinocampholenic acid, 232
Pinocamphone, 146, 222, **226**
— , *cis*- and *trans*- forms of, 229
— , dibromo-derivative, 231
— hydrazone, 102, 232
— , oxidation of, 227
— oximes, 230
— , reduction of, 206
— semicarbazone, 102, 228, 230
— , synthesis of, 130, 228
*iso*Pinocamphone, 229
Pinocamphoric acid, 130, 218, 227
— acid, imide of, 237
Pinocamphylamine, 130, 206, 232
Pinocamphylcarbamide, 232
Pinocarveol, 183, 199, **220**, 231
— , *cis*- and *trans*- forms of, 207, 222
— , derivatives of, 222
— , oxidation of, 222
— , reduction of, 206
Pinocarvone, 183, 185, 199, 221, **240**
— , derivatives of, 242
— , reduction of, 206, 242
Pinol, 107, 137, 201
α-Pinolene, 541
β-Pinolene, *see cyclo*Fenchene

Pinolglycol, 173, 175, 202
Pinolglycolchlorohydrin, 175, 176
Pinolic acid, 149
Pinol oxide, 173
Pinonic acid, 115, 119, 147, 227
— acid, *cis-* and *trans-* forms of, 147
— acid, derivatives of, 148, 149
— acid, oxidation of, 127
— acid, synthesis of, 148
Pinononic acid, 140, 150, 233, 237
— acid, oxime and semicarbazone, 150
Pinophanic acid, 302
Pinoylformic acid, 115, 116, 123, 154
— acid, oxidation of, 127
— acid, phenylhydrazone, 155
Pinus longifolia, oil from, 64
Pinus Merkusii, oil from, 65
Pinus palustris, oil from, 552
Pinus sylvestris L., oil from, 65, 73
Pinylamine, 182, 221
Pistacia Terebinthus L., oil from, 105
*cyclo*Propane-1:1:2-tricarboxylic acid, 287
*cyclo*Propane-1:2:3-tricarboxylic acid, 327
β-*iso*Propyl-δ-acetylvaleronitrile, 443
α-*iso*Propylglutaric acid, 565, 576
β-*iso*Propylglutaric acid, 565
4-*iso*Propyl-Δ^2-*cyclo*hexenone, 19, 195
*iso*Propylidene*cyclo*hexan-4-one, 195
β-*iso*Propyl-levulinic acid, 40
β-*iso*Propylsuccinic acid, 40
Pulegonehydrazone, 61
α- and β-Pyronenes, 134

Reychler's camphorsulphonic acid, *see* Camphor-ω-sulphonic acid

Sabina glycerol, 28
α-Sabina ketol, 17
Sabina ketone, 17, 18, 19, 20, 22
Sabina ketylamine, 19
Sabinene, **16**
— , action of bromine on, 21
— , action of halogen acids on, 21
— , action of isoprene on, 23
— , action of sulphuric acid on, 22
— glycol, 17
— hydrate, 22
— , hydration of, 22
— , oxidation of, 17, 20
— , physical constants of, 19
— , reduction of, 5, 20
Sabinenic acid, 17
Sabinenilanaldehyde, 21
Sabinenilanic acid, 21
Sabinol, **28**
— , action of halogen acids on, 32
— , action of sulphur dioxide on, 32
— , action of sulphuric acid on, 32
— , 3:5-dinitrobenzoate, 29
— , hydrogen phthalate, 30
— , isomerisation to thujone, 31
— , *p*-nitrobenzoate, 29
— , oxidation of, 28, 31
— , physical constants of, 29
— , reduction of, 25, 30
Sage oil, 33
Salvene, 5
Salvia officinalis L., oil from, 33
Salvinol, 33
Sandalwood oil, 242, 251, 264
Santalum album, oil from, 243, 251, 264
Santane, 248
Santene, **243**, 257, 265, 370
— , constitution of, 243
— glycol, 244
— hydrate, 248, 251, **256**
— , hydration of, 250, 252
— hydrochloride, 248, 249, 256
— nitrosate, 250
— nitrosite, 248, 250
— nitrosochloride, 248, 250
— , oxidation of, 243, 244, 249, 257
— , physical constants of, 248
— , reduction of, 248
— , synthesis of, 245, 248
— tribromide, 249
Santenenic acid, 255
Santenic acid and stereoisomers, 253, 254, 257, 259, 262
— acid, synthesis of, 254
*allo*Santenic acid, 254
*iso*Santenic acid, 254
Santenol, 248, 250, **251**, 265
— , action of phosphorus pentachloride on, 255
— , hydrogen diphenate, 253
— , oxidation of, 251, 253
— , phenylurethane, 253
— , stereoisomers of, 253
γ-Santenol, 249, 256
Santenone, 251, **257**, 432
— , action of methyl magnesium iodide on, 263
— , benzylidene derivative, 261
— hydrazone, 261
— , hydroxymethylene derivative, 262
— , oxidation of, 257, 260, 262
— oxime, 260
— , pernitroso-derivative, 261

Santenone, reduction of, 251, 260
— semicarbazone, 258, 259, 261
— , stereoisomers of, 259
— , synthesis of, 258
*iso*Santenone, 261
α-Santenone, 259
β-Santenone, 259
Santenone alcohol, 251
β-Santenone alcohol, 253
Santenonecarboxylic acid, 262
Santenonequinone, 261, 262
Santenylamine, 260
Santolide, 258
Savin, oil of, 16, 28
Sobreroerythritol, 175
Sobrerol, 107, 137, 143
— dichloride, 173
Sulphocamphylic acid, 499
— acid, conversion into *iso*lauronolic acid, 500
-Sulpho-αα-dimethylglutaric acid, 499
Sylvestrene dihydrochloride, 65

Tanacetone, 33
-Tanacetonedicarboxylic acid, 33
Tanacetophorone, 39
Tanacetum vulgare L., oil from, 33
Tansy oil, 33
Terebic acid, 71, 78, 110, 144
Teresantalal, 266, 337
Teresantalic acid, **264**, 337
— acid, action of formic acid on, 251, 265
— acid, action of hydrogen chloride on, 266
— acid, action of sulphuric acid on, 248, 265
— acid, constitution of, 266
*iso*Teresantalic acid, 269
— acid, reduction of, 269
Teresantalol, **264**, 337
— , action of hydrogen chloride on, 270
— , action of sulphuric acid on, 270
— , oxidation of, 266
— , physical constants of, 270
Teresantalyl chloride, 266
Terpenylic acid, 70, 110, 143
Terpin hydrate, 166
1:4-Terpin, 13
Terpinene dihydrochloride, 12
Terpinene-4-ol, 13
α-Terpineol, 167
1:2:3:4-Tetrabromo-*p*-menthane, 20
Tetrahydroeucarveol, 88, 91
Tetrahydroeucarvone, 88, 91
Tetrahydroeucarvoxime, 93
Tetrahydroeucarvylamine, 93, 94
Tetrahydroumbellulol, 59
Tetrahydroumbellulone, 59
Tetramercuritricamphor di-iodide, 409
ααγγ-Tetramethylglutaric acid, 583
1:1:2:5-Tetramethyl-Δ^4-*cyclo*penten-3-one, 393
Thioborneol, 365, 446
Thiocamphor, 365, 446
Thuja occidentalis, oil from, 33, 561
α-Thujadicarboxylic acid, 12, 19, 28, 37
— acid, synthesis from umbellularic acid, 57
β-Thujadicarboxylic acid, 39
Thuja ketone, 37
α-Thujaketonic acid, 12, 33, 36
— acid, synthesis of, 37
β-Thujaketonic acid, 33, 37, 38
α- and β-Thujamenthol, 41, 42
α- and β-Thujamenthone, 41, 42
Thujane, **5**, 13, 16, 30
— , action of bromine and hydrogen bromide on, 8
— , action of sulphuric acid on, 10
— , oxidation of, 8
— , physical constants of, 8
— , reduction of, 8
— , synthesis of, 6
α-Thujene, **10**, 27
— , action of hydrogen halides on, 13
— , action of sulphuric acid on, 13
— , hydration of, 13
— nitrolbenzylamine, 10
— nitrolpiperidide, 10, 12
— nitrosochloride, 10, 12
— , oxidation of, 12, 13
— , physical constants of, 12
— , reduction of, 5, 13
β-Thujene, **14**, 28
— , oxidation of, 15
— , reduction of, 5, 15
Thujone, 26, **32**
— , action of Grignard reagent on, 51
— , action of halogens on, 47
— , benzylidene derivative, 51
— , bisulphite compound, 47
— , constitution of, 34
— , conversion into "Isothujon", 39, 46
— 2:4-dinitrophenylhydrazone, 43, 45

Thujone, enolic form of, 46
— , formation by isomerisation of sabinol, 31
— hydrazone, 5, 50
— , hydroxymethylene derivative, 35, 51
— *p*-nitrophenylhydrazone, 43
— , oxidation of, 33, 35, 47
— oxime, 47
— , physical constants of, 45
— , reactions of active methylene group in, 50
— , reduction of, 24, 46
— semicarbazone, 43, 45, 50
— , synthesis from α-thujaketonic acid, 43
*iso*Thujone (*see also* Thujone), 26, 43, 45
— , reduction of, 24
Thujoneisoxime, 49
Thujyl alcohol, 23
— alcohol, action of halogen acids on, 26
— alcohol, 3:5-dinitrobenzoates, 25
— alcohol, hydrogen phthalates, 24
— alcohol, *p*-nitrobenzoates, 25
— alcohol, oxidation of, 25
— alcohol, physical constants of, 25
— alcohol, stereoisomers of, 24
*iso*Thujyl alcohol, 24
*neo*Thujyl alcohol, 24, 31
Thujylamine, 48
Thujyl chloride, 11, 26
Thujylhydrazine, 5
Thujyltrimethylammonium hydroxide, 11, 49
αα′π-Tribromocamphor, 408, 409
αα′ω-Tribromocamphor, 407, 409
Tribromofenchane, 572
Tricyclal, 312, 335
Tricyclene, 158, 266, 314, 324, 333
— , action of halogens on, 338
— , action of hydrogen chloride on, 308, 339
— , action of nitric acid on, 314, 339
— , hydration of, 339
— , physical constants of, 338
— , reduction of, 338
*iso*Tricyclene, 329
Tricyclenic acid, 298, 311, 334, 368
Tricyclenone, 314
Tricyclol, 335
2:2:3-Trimethyl*cyclo*hexan-4-one-1-carboxylic acid, 468, 469
1:3:3-Trimethyl-Δ^1-*cyclo*hexene-4-carboxylic acid, 97
2:2:3-Trimethyl*cyclo*pentanecarboxylic acid, 445
1:2:2-Trimethyl*cyclo*pentane-3:5-dicarboxylic acid, 278
1:1:2-Trimethyl-Δ^2-*cyclo*pentene-5-carboxylic acid, *see* α-Campholytic acid
2:3:3-Trimethyl-Δ^1-*cyclo*pentene-1-carboxylic-4-sulphonic acid, *see* Sulphocamphylic acid
αα*β*-Trimethyltricarballylic acid, *see* Camphoronic acid

Umbellularia Californica Nuttal, oil from, 52
Umbellularic acid, 53
— acid, synthesis of, 56
Umbellulone, 52
— , constitution of, 53
— dibromide, 58
— hydroxylamino-oxime, 60
— , oxidation of, 53
— , physical constants of, 57
— , reduction of, 54, 57
— semicarbazido-semicarbazone, 57, 60
— semicarbazone, 60
— thiosemicarbazido-semicarbazone, 60
Umbellulonic acid, 53
— acid, oxime, 53
— acid, synthesis of, 57

Valerian, oil of, 350
Valeriana officinalis L., oil from, 350
Verbanol, 216, 235, 237
— , dehydration of, 218
— , hydrogen phthalates, 217
— , stereoisomers of, 217
Verbanone, 235
— , conversion into pinocamphone, 228
— , dibenzylidene derivative, 237
— , hydration of, 237
— hydrazone, 102, 236
— , oxidation of, 236
— oxime, 235
— semicarbazone, 235
— , synthesis of, 235
Verbanone-2-carboxylic acid, 228
Verbanylamine, 239
Verbena oil, 233
Verbena triphylla L., oil from, 233
Verbenene, 218
— dibromide, 219
Verbenol, 214
— , *cis*- and *trans*- forms of, 216
— , dehydration of, 218

Verbenol, *p*-nitrobenzoates, 216
— , oxidation of, 215, 216
— , reduction of, 216
Verbenone, 215, **232**, 236
— , action of hydrogen chlorides on, 237
— , compound with sodium sulphite, 235
— hydroxylamino-oxime, 239
— , oxidation of, 233, 237
— oxide, 237
— oxime, reduction of, 239
— ozonides, 140
— , physical constants of, 234
Verbenone, pinacone from, 237
— , reduction of, 215, 237
— semicarbazone, 234
Verbenyl bromide, 169
Vestrylamine hydrochloride, 81

Wagner-Meerwein isomerisation, 156
Wormwood oil, 33

Zanthoxylum Budrunga Wall., oil from, 16
Zieria Smithii, oil from, 95